(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) **EP 3 181 081 A1**

(12) **EUROPEAN PATENT APPLICATION**

(43) Date of publication:
21.06.2017 Bulletin 2017/25

(21) Application number: **16197774.9**

(22) Date of filing: **11.03.2013**

(51) Int Cl.:
A61B 18/14 *(2006.01)* ***A61M 25/01*** *(2006.01)*
A61B 18/00 *(2006.01)* *A61M 25/09* *(2006.01)*

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR

(30) Priority: **11.05.2012 US 201261646218 P**

(62) Document number(s) of the earlier application(s) in accordance with Art. 76 EPC:
13715790.5 / 2 846 724

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Remarks:
•This application was filed on 08.11.2016 as a divisional application to the application mentioned under INID code 62.
•Claims filed after the date of filing of the application / after the date of receipt of the divissional application (Rule68(4) EPC)

(54) **MULTI-ELECTRODE CATHETER ASSEMBLIES FOR RENAL NEUROMODULATION AND ASSOCIATED SYSTEMS**

(57) Catheter apparatuses and systems for achieving renal neuromodulation by intravascular access are disclosed herein. One aspect of the present technology, for example, is directed to a treatment device having a multi-electrode array configured to be delivered to a renal blood vessel. The array is selectively transformable between a delivery or low-profile state (e.g., a generally straight shape) and a deployed state (e.g., a radially expanded, generally spiral/helical shape). The multi-electrode array is sized and shaped so that the electrodes or energy delivery elements contact an interior wall of the renal blood vessel when the array is in the deployed (e.g., spiral/helical) state. The electrodes or energy delivery elements are configured for direct and/or indirect application of thermal and/or electrical energy to heat or otherwise electrically modulate neural fibers that contribute to renal function.

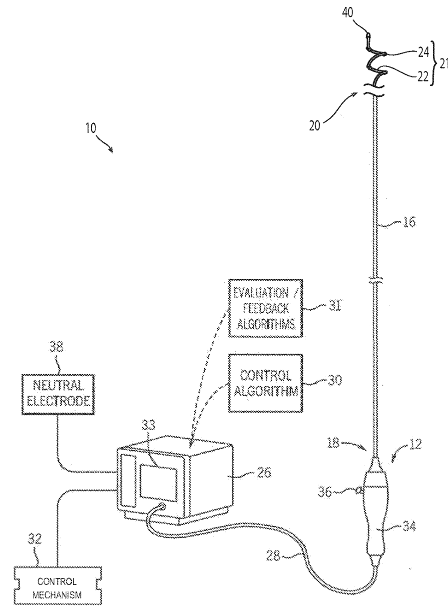

FIG. 1

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Description

CROSS REFERENCE TO RELATED APPLICATION(S)

[0001] The present application claims the benefit of and priority to U.S. Provisional Patent Application No. 61/646,218, filed May 11, 2012, which is incorporated herein by reference in its entirety.

ADDITIONAL APPLICATIONS INCORPORATED BY REFERENCE

[0002] The following applications are also incorporated herein by reference in their entireties:

U.S. Patent Application No. 13/281,360, filed October 25, 2011;

U.S. Patent Application No. 13/281,361, filed October 25, 2011; and

U.S. Patent Application No. 13/281,395, filed October 25, 2011.

[0003] As such, components and features of embodiments disclosed in these applications may be combined with various components and features disclosed in the present application.

TECHNICAL FIELD

[0004] The present technology relates generally to renal neuromodulation and associated systems and methods. In particular, several embodiments are directed to multi-electrode radio frequency (RF) ablation catheter assemblies for intravascular renal neuromodulation and associated systems and methods.

BACKGROUND

[0005] The sympathetic nervous system (SNS) is a primarily involuntary bodily control system typically associated with stress responses. Fibers of the SNS innervate tissue in almost every organ system of the human body and can affect characteristics such as pupil diameter, gut motility, and urinary output. Such regulation can have adaptive utility in maintaining homeostasis or preparing the body for rapid response to environmental factors. Chronic activation of the SNS, however, is a common maladaptive response that can drive the progression of many disease states. Excessive activation of the renal SNS in particular has been identified experimentally and in humans as a likely contributor to the complex pathophysiology of hypertension, states of volume overload (such as heart failure), and progressive renal disease. For example, radiotracer dilution has demonstrated increased renal norepinephrine ("NE") spillover rates in patients with essential hypertension.

[0006] Cardio-renal sympathetic nerve hyperactivity can be particularly pronounced in patients with heart failure. For example, an exaggerated NE overflow from the heart and kidneys of plasma is often found in these patients. Heightened SNS activation commonly characterizes both chronic and end stage renal disease. In patients with end stage renal disease, NE plasma levels above the median have been demonstrated to be predictive of cardiovascular diseases and several causes of death. This is also true for patients suffering from diabetic or contrast nephropathy. Evidence suggests that sensory afferent signals originating from diseased kidneys are major contributors to initiating and sustaining elevated central sympathetic outflow.

[0007] Sympathetic nerves innervating the kidneys terminate in the blood vessels, the juxtaglomerular apparatus, and the renal tubules. Stimulation of the renal sympathetic nerves can cause increased renin release, increased sodium (Na+) reabsorption, and a reduction of renal blood flow. These neural regulation components of renal function are considerably stimulated in disease states characterized by heightened sympathetic tone and likely contribute to increased blood pressure in hypertensive patients. The reduction of renal blood flow and glomerular filtration rate as a result of renal sympathetic efferent stimulation is likely a cornerstone of the loss of renal function in cardio-renal syndrome (i.e., renal dysfunction as a progressive complication of chronic heart failure). Pharmacologic strategies to thwart the consequences of renal efferent sympathetic stimulation include centrally acting sympatholytic drugs, beta blockers (intended to reduce renin release), angiotensin converting enzyme inhibitors and receptor blockers (intended to block the action of angiotensin II and aldosterone activation consequent to renin release), and diuretics (intended to counter the renal sympathetic mediated sodium and water retention). These pharmacologic strategies, however, have significant limitations including limited efficacy, compliance issues, side effects, and others. Recently, intravascular devices that reduce sympathetic nerve activity by applying an energy field to a target site in the renal blood vessel (e.g., via RF ablation) have been shown to reduce blood pressure in patients with treatment-resistant hypertension.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] Many aspects of the present disclosure can be better understood with reference to the following drawings. The components in the drawings are not necessarily to scale. Instead, emphasis is placed on illustrating clearly the principles of the present disclosure. Furthermore, components can be shown as transparent in certain views for clarity of illustration only and not to indicate that the illustrated component is necessarily transparent.

FIG. 1 is a partially schematic diagram of a neuromodulation system configured in accordance with an embodiment of the present technology.

FIG. 2 illustrates modulating renal nerves with a multi-electrode catheter configured in accordance with an embodiment of the present technology.

FIG. 3A is a side view of a distal portion of a catheter having a therapeutic assembly or treatment section in a delivery state (e.g., low-profile or collapsed configuration) outside a patient in accordance with an embodiment of the present technology.

FIG. 3B is a perspective view of the distal portion of the catheter of FIG. 3A in a deployed state (e.g., expanded configuration) outside the patient.

FIG. 4 is an enlarged view of a portion of the treatment device of FIG. 3A.

FIG. 5 is a partially schematic side view of a loading tool configured in accordance with an embodiment of the present technology.

FIG. 6 is a conceptual diagram illustrating the sympathetic nervous system and how the brain communicates with the body via the sympathetic nervous system.

FIG. 7 is an enlarged anatomical view illustrating nerves innervating a left kidney to form a renal plexus surrounding a left renal artery.

FIGS. 8A and 8B are anatomical and conceptual views, respectively, illustrating a human body including a brain and kidneys and neural efferent and afferent communication between the brain and kidneys.

FIGS. 9A and 9B are anatomic views illustrating, respectively, an arterial vasculature and a venous vasculature of a human.

DETAILED DESCRIPTION

[0009] The present technology is directed to apparatuses, systems, and methods for achieving electrically- and/or thermally-induced renal neuromodulation (i.e., rendering neural fibers that innervate the kidney inert or inactive or otherwise completely or partially reduced in function) by percutaneous transluminal intravascular access. In particular, embodiments of the present technology relate to catheters and catheter assemblies having multi-electrode arrays and being movable between a delivery or low-profile state (e.g., a generally straight shape) and a deployed state (e.g., a radially expanded, generally helical shape). The electrodes or energy delivery elements comprising the multi-electrode array are configured to deliver energy (e.g., electrical energy, RF energy, pulsed electrical energy, thermal energy) to a renal artery after being advanced thereto via a catheter along a percutaneous transluminal path (e.g., a femoral artery puncture, an iliac artery and the aorta, a radial artery, or another suitable intravascular path). The catheter or catheter assembly carrying the multi-electrode array is sized and shaped so that the electrodes or energy delivery elements contact an interior wall of the renal artery when the catheter is in the deployed (e.g., helical) state within the renal artery. In addition, the helical shape of the deployed portion of the catheter carrying the array allows blood to flow through the helix, which is expected to help prevent occlusion of the renal artery during activation of the energy delivery element. Further, blood flow in and around the array may cool the associated energy delivery elements and/or the surrounding tissue. In some embodiments, cooling the energy delivery elements allows for the delivery of higher power levels at lower temperatures than may be reached without cooling. This feature is expected to help create deeper and/or larger lesions during therapy, reduce intimal surface temperature, and/or allow longer activation times with reduced risk of overheating during treatment.

[0010] Specific details of several embodiments of the technology are described below with reference to FIGS. 1-9B. Although many of the embodiments are described below with respect to devices, systems, and methods for intravascular modulation of renal nerves using multi-electrode arrays, other applications and other embodiments in addition to those described herein are within the scope of the technology. Additionally, several other embodiments of the technology can have different configurations, components, or procedures than those described herein. A person of ordinary skill in the art, therefore, will accordingly understand that the technology can have other embodiments with additional elements, or the technology can have other embodiments without several of the features shown and described below with reference to FIGS. 1-9B.

[0011] As used herein, the terms "distal" and "proximal" define a position or direction with respect to the treating clinician or clinician's control device (e.g., a handle assembly). "Distal" or "distally" are a position distant from or in a direction away from the clinician or clinician's control device. "Proximal" and "proximally" are a position near or in a direction toward the clinician or clinician's control device.

1. <u>Renal Neuromodulation</u>

[0012] Renal neuromodulation is the partial or complete incapacitation or other effective disruption of nerves innervating the kidneys. In particular, renal neuromodulation comprises inhibiting, reducing, and/or blocking neural communication along neural fibers (i.e., efferent and/or afferent nerve fibers) innervating the kidneys. Such incapacitation can be long-term (e.g., permanent or for periods of months, years, or decades) or short-term (e.g., for periods of minutes, hours, days, or weeks). Renal neuromodulation is expected to efficaciously treat several clinical conditions characterized by increased overall sympathetic activity, and in particular conditions associated with central sympathetic over stimulation such as hypertension, heart failure, acute myocardial infarction, metabolic syndrome, insulin resistance, diabetes, left ventricular hypertrophy, chronic and end stage renal disease, inappropriate fluid retention in heart failure, cardio-renal syndrome, osteoporosis, and sudden death. The reduction of afferent neural signals contributes to the systemic reduction of sympathetic tone/drive, and renal neuromodulation is expected to be useful in treating several conditions associated with systemic sympathetic over activity or hyperactivity. Renal neuromodulation can potentially benefit a variety of organs and bodily structures innervated by sympathetic nerves.

[0013] Various techniques can be used to partially or completely incapacitate neural pathways, such as those innervating the kidney. The purposeful application of energy (e.g., electrical energy, thermal energy) to tissue by energy delivery element(s) can induce one or more desired thermal beating effects on localized regions of the renal artery and adjacent regions of the renal plexus, which lay intimately within or adjacent to the adventitia of the renal artery. The purposeful application of the thermal heating effects can achieve neuromodulation along all or a portion of the renal plexus.

[0014] The thermal heating effects can include both thermal ablation and non-ablative thermal alteration or damage (e.g., via sustained heating and/or resistive heating). Desired thermal heating effects may include raising the temperature of target neural fibers above a desired threshold to achieve non-ablative thermal alteration, or above a higher temperature to achieve ablative thermal alteration. For example, the target temperature can be above body temperature (e.g., approximately 37°C) but less than about 45°C for non-ablative thermal alteration, or the target temperature can be about 45°C or higher for the ablative thermal alteration.

[0015] More specifically, exposure to thermal energy (heat) in excess of a body temperature of about 37°C, but below a temperature of about 45°C, may induce thermal alteration via moderate heating of the target neural fibers or of vascular structures that perfuse the target fibers. In cases where vascular structures are affected, the target neural fibers are denied perfusion resulting in necrosis of the neural tissue. For example, this may induce non-ablative thermal alteration in the fibers or structures. Exposure to heat above a temperature of about 45°C, or above about 60°C, may induce thermal alteration via substantial heating of the fibers or structures. For example, such higher temperatures may thermally ablate the target neural fibers or the vascular structures. In some patients, it may be desirable to achieve temperatures that thermally ablate the target neural fibers or the vascular structures, but that are less than about 90°C, or less than about 85°C, or less than about 80°C, and/or less than about 75°C. Regardless of the type of heat exposure utilized to induce the thermal neuromodulation, a reduction in renal sympathetic nerve activity (RSNA) is expected.

II. Selected Embodiments of Neuromodulation Systems

[0016] FIG. 1 illustrates a renal neuromodulation system 10 ("system 10") configured in accordance with an embodiment of the present technology. The system 10 includes an intravascular catheter 12 operably coupled to an energy source or energy generator 26 (e.g., a RF energy generator). The catheter 12 can include an elongated shaft 16 having a proximal portion 18, a handle 34 at a proximal region of the proximal portion 18, and a distal portion 20. The catheter 12 can further include a therapeutic assembly or treatment section 21 (shown schematically) at the distal portion 20 (e.g., attached to the distal portion 20, defining a section of the distal portion 20, etc.). As explained in further detail below, the therapeutic assembly 21 can include a support structure 22 and an array of two or more energy delivery elements 24 (e.g., electrodes) configured to be delivered to a renal blood vessel (e.g., a renal artery) in a low-profile configuration. Upon delivery to the target treatment site within the renal blood vessel, the therapeutic assembly 21 is further configured to be deployed into an expanded state (e.g., a generally spiral/helical configuration) for delivering energy at the treatment site and providing therapeutically-effective electrically- and/or thermally-induced renal neuromodulation. Alternatively, the deployed state may be non-helical provided that the deployed state delivers the energy to the treatment site. The therapeutic assembly 21 may be transformed between the delivery and deployed states using a variety of suitable mechanisms or techniques (e.g., self-expansion, remote actuation via an actuator, etc.).

[0017] The proximal end of the therapeutic assembly 21 is carried by or affixed to the distal portion 20 of the elongated shaft 16. A distal end of the therapeutic assembly 21 may terminate the catheter 12 with, for example, an atraumatic tip 40. In some embodiments, the distal end of the therapeutic assembly 21 may also be configured to engage another element of the system 10 or catheter 12. For example, the distal end of the therapeutic assembly 21 may define a passageway for receiving a guide wire (not shown) for delivery of the treatment device using over-the-wire ("OTW") or rapid exchange ("RX") techniques. Further details regarding such arrangements are described below.

[0018] The catheter 12 can be electrically coupled to the energy source 26 via a cable 28, and the energy source 26 (e.g., a RF energy generator) can be configured to produce a selected modality and magnitude of energy for delivery to the treatment site via the energy delivery elements 24. As described in greater detail below, supply wires (not shown) can extend along the elongated shaft 16 or through a lumen in the shaft 16 to the individual energy delivery elements 24 and transmit the treatment energy to the energy delivery elements 24. In some embodiments, each energy delivery element 24 includes its own supply wire. In other embodiments, however, two or more energy delivery elements 24 may be electrically coupled to the same supply wire. A control mechanism 32, such as foot pedal or handheld remote control device, may be connected to the energy source 26 to allow the clinician to initiate, terminate and, optionally, adjust various operational characteristics of the energy source 26, including, but not limited to, power delivery. The remote control device (not shown) can be positioned in a sterile field and operably coupled to the energy delivery elements 24, and can be configured to allow the clinician to selectively activate and deactivate the energy delivery elements 24. In other embodiments, the remote control device may be built into the handle assembly 34.

[0019] The energy source or energy generator 26 can be configured to deliver the treatment energy via an automated control algorithm 30 and/or under the control of a clinician. For example, the energy source 26 can include computing devices (e.g., personal computers, server computers, tablets, etc.) having processing circuitry (e.g., a microprocessor) that is configured to execute stored instructions relating to the control algorithm 30. In addition, the processing circuitry may be configured to execute one or more evaluation/feedback algorithms 31, which can be communicated to the clinician. For example, the energy source 26 can include a monitor or display 33 and/or associated features that are configured to provide visual, audio, or other indications of power levels, sensor data, and/or other feedback. The energy source 26 can also be configured to communicate the feedback and other information to another device, such as a monitor in a catheterization laboratory.

[0020] The energy delivery elements 24 may be configured to deliver power independently (i.e., may be used in a monopolar fashion), either simultaneously, selectively, or sequentially, and/or may deliver power between any desired combination of the elements (i.e., may be used in a bipolar fashion). In monopolar embodiments, a neutral or dispersive electrode 38 may be electrically connected to the energy generator 26 and attached to the exterior of the patient (e.g., as shown in FIG. 2). Furthermore, the clinician optionally may choose which energy delivery element(s) 24 are used for power delivery in order to form highly customized lesion(s) within the renal artery having a variety of shapes or patterns. In still other embodiments, the system 10 can be configured to deliver other suitable forms of treatment energy, such as a combination of monopolar and bipolar electric fields.

[0021] In several embodiments, the energy source 26 may include a radio-frequency identification (RFID) evaluation module (not shown) mounted at or near one or more ports on the energy source 26 and configured to wirelessly read and write to one or more RFID tags (not shown) on the catheter 12. In one particular embodiment, for example, the catheter 12 may include an RFID tag housed within or otherwise attached to the connector portion of the cable 28 that is coupled to the energy source 26. The RFID tag can include, for example, an antenna and an RFID chip for processing signals, sending/receiving RF signals, and storing data in memory. Suitable RFID tags include, for example, MB89R118 RFID tags available from Fujitsu Limited of Tokyo, Japan. The memory portion of the RFID tag can include a plurality of blocks allocated for different types of data. For example, a first memory block can include a validation identifier (e.g., a unique identifier associated with the specific type of catheter and generated from the unique ID of the RFID tag using an encrypting algorithm), and a second memory block can be allocated as a catheter usage counter that can be read and then written to by the RFID module carried by the energy source 26 after catheter use. In other embodiments, the RFID tag can include additional memory blocks allocated for additional catheter usage counters (e.g., to allow the catheter 12 to be used a specific limited number of times) and/or other information associated with the catheter 12 (e.g., lot number, customer number, catheter model, summary data, etc.).

[0022] The RFID evaluation module carried by the energy source 26 can include an antenna and a processing circuit that are together used to communicate with one or more portions of the energy source 26 and wirelessly read/write to one or more RFID tag within its proximity (e.g., when the cable 28 including an RFID tag is attached to the energy source 26). Suitable RFID evaluation modules include, for example, a TRF7960A Evaluation Module available from Texas Instruments Incorporated of Dallas, Texas.

[0023] In operation, the RFID evaluation module is configured to read information from the RFID tag (carried by the cable 28 or another suitable portion of the catheter 12), and communicate the information to software of the energy source 26 to validate the attached catheter 12 (e.g., validate that the catheter 12 is compatible with the energy source 26), read the number of previous uses associated with the particular catheter 12, and/or write to the RFID tag to indicate catheter use. In various embodiments, the energy source 26 may be configured to disable energy delivery to the catheter 12 when predefined conditions of the RFID tag are not met. For example, when each the catheter 12 is connected to the energy source 26, the RFID evaluation module can read a unique anti-counterfeit number in an encrypted format from the RFID tag, decrypt the number, and then authenticate the number and the catheter data format for recognized catheters (e.g., catheters that are compatible with the particular energy source 26, non-counterfeit catheters, etc.). In various embodiments, the RFID tag can include identifier(s) that correspond to a specific type of catheter, and the RFID evaluation module can transmit this information to a main controller of the energy source 26, which can adjust the settings (e.g., the control algorithm 30) of the energy source 26 to the desired operating parameters/characteristics (e.g., power levels, display modes, etc.) associated with the specific catheter. Further, if the RFID evaluation module identifies the catheter 12 as counterfeit or is otherwise unable to identify the catheter 12, the energy source 26 can automatically disable the use of the catheter 12 (e.g., preclude energy delivery).

[0024] Once the catheter 12 has been identified, the RFID evaluation module can read the RFID tag memory address spaces to determine if the catheter 12 was previously connected to a generator (i.e., previous used). In certain embodiments, the RFID tag may limit the catheter 12 to a single use, but in other embodiments the RFID tag can be configured to provide for more than one use (e.g., 2 uses, 5 uses, 10 uses, etc.). If the RFID evaluation module recognizes that the catheter 12 has been written (i.e., used) more than a predetermined use limit, the RFID module can communicate with the energy source 26 to disable energy delivery to the catheter 12. In certain embodiments, the RFID evaluation module can be configured to interpret all the catheter connections to an energy source within a predefined time period (e.g., 5 hours, 10 hours, 24 hours, 30 hours, etc.) as a single connection (i.e., a single use), and allow the catheter 12 to be used multiple times within the predefined time period. After the catheter 12 has been detected, recognized, and judged as a "new connection" (e.g., not used more than the predefined limit), the RFID evaluation module can write to the RFID tag (e.g., the time and date of the system use and/or other information) to indicate that the catheter 12 has been used. In other embodiments, the RFID evaluation module and/or RFID tag may have different features and/or different configurations.

[0025] The system 10 can also include one or more sensors (not shown) located proximate to or within the energy delivery elements 24. For example, the system 10 can include temperature sensors (e.g., thermocouple, thermistor, etc.), impedance sensors, pressure sensors, optical sensors, flow sensors, and/or other suitable sensors connected to one or more supply wires (not shown) that transmit signals from the sensors and/or convey energy to the energy delivery elements 24.FIG. 2 (with additional reference to FIG. 1) illustrates modulating renal nerves with an embodiment of the system 10. The catheter 12 provides access to the renal plexus RP through an intravascular path P, such as a percutaneous access site in the femoral (illustrated), brachial, radial, or axillary artery to a targeted treatment site within a respective renal artery RA. As illustrated, a section of the proximal portion 18 of the shaft 16 is exposed externally of the patient. By manipulating the proximal portion 18 of the shaft 16 from outside the intravascular path P, the clinician may advance the shaft 16 through the sometimes tortuous intravascular path P and remotely manipulate the distal portion 20 of the shaft 16. In the embodiment illustrated in FIG. 2, the therapeutic assembly 21 is delivered intravascularly to the treatment site using a guide wire 66 in an OTW technique. As noted previously, the distal end of the therapeutic assembly 21 may define a lumen or passageway for receiving the guide wire 66 for delivery of the catheter 12 using either OTW or RX techniques. At the treatment site, the guide wire 66 can be at least partially axially withdrawn or removed, and the therapeutic assembly 21 can transform or otherwise be moved to a deployed arrangement for delivering energy at the treatment site. Further details regarding such arrangements are described below with reference to FIGS. 3A and 3B. The guide wire 66 may comprise any suitable medical guide wire sized to slidably fit within the lumen. In one particular embodiment, for example, the guide wire 66 may have a diameter of 0.356 mm (0.014 inch). In other embodiments, the therapeutic assembly 21 may be delivered to the treatment site within a guide sheath (not shown) with or without using the guide wire 66. When the therapeutic assembly 21 is at the target site, the guide sheath may be at least partially withdrawn or retracted and the therapeutic assembly 21 can be transformed into the deployed arrangement. Additional details regarding this type of configuration are described below. In still other embodiments, the shaft 16 may be steerable itself such that the therapeutic assembly 21 may be delivered to the treatment site without the aid of the guide wire 66 and/or guide sheath.

[0026] Image guidance, e.g., computed tomography (CT), fluoroscopy, intravascular ultrasound (IVUS), optical coherence tomography (OCT), intracardiac echocardiography (ICE), or another suitable guidance modality, or combinations thereof, may be used to aid the clinician's positioning and manipulation of the therapeutic assembly 21. For example, a fluoroscopy system (e.g., including a flat-panel detector, x-ray, or c-arm) can be rotated to accurately visualize and identify the target treatment site. In other embodiments, the treatment site can be determined using IVUS, OCT, and/or other suitable image mapping modalities that can correlate the target treatment site with an identifiable anatomical structure (e.g., a spinal feature) and/or a radiopaque ruler (e.g., positioned under or on the patient) before delivering the catheter 12. Further, in some embodiments, image guidance components (e.g., IVUS, OCT) may be integrated with the catheter 12 and/or run in parallel with the catheter 12 to provide image guidance during positioning of the therapeutic assembly 21. For example, image guidance components (e.g., IVUS or OCT) can be coupled to at least one of the therapeutic assembly 21 (e.g., proximal to the therapeutic arms 25) to provide three-dimensional images of the vasculature proximate the target site to facilitate positioning or deploying the multi-electrode assembly within the target renal blood vessel.

[0027] The purposeful application of energy from the energy delivery elements 24 may then be applied to target tissue to induce one or more desired neuromodulating effects on localized regions of the renal artery and adjacent regions of the renal plexus RP, which lay intimately within, adjacent to, or in close proximity to the adventitia of the renal artery RA. The purposeful application of the energy may achieve neuromodulation along all or at least a portion of the renal plexus RP. The neuromodulating effects are generally a function of, at least in part, power, time, contact between the energy delivery elements 24 (FIG. 1) and the vessel wall, and blood flow through the vessel. The neuromodulating effects may include denervation, thermal ablation, and/or non-ablative thermal alteration or damage (e.g., via sustained heating and/or resistive heating). Desired thermal heating effects may include raising the temperature of target neural fibers above a desired threshold to achieve non-ablative thermal alteration, or above a higher temperature to achieve ablative thermal alteration. For example, the target temperature may be above body temperature (e.g., approximately 37°C) but less than about 45°C for non-ablative thermal alteration, or the target temperature may be about 45°C or higher for the ablative thermal alteration. Desired non-thermal neuromodulation effects may include altering the electrical signals transmitted in a nerve.

[0028] FIG. 3A is a side view of the distal portion 20 of the catheter 12 and the therapeutic assembly or treatment section 21 in a delivery state (e.g., low-profile or collapsed configuration) outside a patient, and FIG. 3B is a perspective view of the therapeutic assembly 21 in a deployed state (e.g., expanded configuration) outside the patient. As described previously, the catheter 12 may be configured for OTW delivery from an access site in which the guide wire 66 (FIG. 2) is initially inserted to a treatment site (e.g., within a renal artery), and the catheter 12 is installed over the guide wire. As described in greater detail below, a guide wire may be either inserted into or at least partially withdrawn from the distal portion 20 to transform the therapeutic assembly 21 between the delivery state (FIG. 3A) and the deployed state (FIG. 3B). For example, as shown in FIG. 3A, a guide wire (not shown) extending through at least a portion of the length of the catheter 12 may be configured to straighten a pre-shaped spiral/helical control member 50 (shown schematically in broken lines) of the catheter 12 during delivery, and the guide wire may be at least partially withdrawn or slidably moved relative to the distal portion 20 to allow the therapeutic assembly 21 to transform to the deployed state (FIG. 3B).

[0029] As best seen in FIG. 3A, the therapeutic assembly 21 includes multiple (e.g., four, five, etc.) energy delivery elements 24 carried by the support structure 22. In this embodiment, the support structure 22 comprises a flexible tube 42 and the pre-shaped control member 50 within the tube 42. The flexible tube 42 may be composed of a polymer material such as polyamide, polyimide, polyether block amide copolymer sold under the trademark PEBAX, polyethylene terephthalate (PET), polypropylene, aliphatic, polycarbonate-based thermoplastic polyurethane sold under the trademark CARBOTHANE, or a polyether ether ketone (PEEK) polymer that provides the desired flexibility. In other embodiments, however, the tube 42 may be composed of other suitable materials.

[0030] As mentioned above, the pre-shaped control member 50 may be used to provide a spiral/helical shape to the relatively flexible distal portion 20 of the catheter 12. As best seen in FIG. 3B, for example, the control member 50 is a tubular structure comprising a nitinol multifilar stranded wire with a lumen therethrough and sold under the trademark HELICAL HOLLOW STRAND (HHS), and commercially available from Fort Wayne Metals of Fort Wayne, Indiana. The tubular control member 50 may be formed from a variety of different types of materials, may be arranged in a single or dual-layer configuration, and may be manufactured with a selected tension, compression, torque and pitch direction. The HHS material, for example, may be cut using a laser, electrical discharge machining (EDM), electrochemical grinding (ECG), or other suitable means to achieve a desired finished component length and geometry. For example, as best seen in FIG. 3B, the control member 50 in the present embodiment has a pre-set spiral/helical configuration that defines the deployed state of the therapeutic assembly 21 such that the energy delivery elements 24 of the therapeutic assembly 21 are offset from each other (e.g., both angularly and longitudinally offset relative to a longitudinal axis of the renal artery) and may be positioned in stable apposition with a wall of the renal artery (FIG. 2) for treatment. For purposes of clarification, the pre-set helical shape of the therapeutic assembly 21 in its deployed state may be defined by dimensions (e.g., helix diameter and pitch) that are distinct from the dimensions (e.g., helix diameter and pitch) of the HHS itself. In other words, the multifilar hollow tube forming control member 50 is itself pre-set into a helical shape.

[0031] Forming the control member 50 of nitinol multifilar stranded wire(s) or other similar materials is expected to eliminate the need for any additional reinforcement wire(s) or structures within the support structure 22 to provide a desired level of support and rigidity to the therapeutic assembly 21. This feature is expected to reduce the number of manufacturing processes required to form the catheter 12 and reduce the number of materials required for the device. Another feature of the therapeutic assembly 21 is that the control member 50 and inner wall of the tube 42 are in intimate contact and there is little or no space between the control member 50 and the tube 42 (as best seen in FIG. 4). In one embodiment, for example, tube 42 can be expanded prior to assembly such that applying hot air to the tube 42 during the manufacturing process can shrink the tube onto the control member 50, as will be understood by those familiar with the ordinary use of shrink tubing materials. This feature is expected to inhibit or eliminate wrinkles or kinks that might occur in the tube 42 as the therapeutic assembly 21 transforms from the relatively straight delivery state to the deployed, generally helical state.

[0032] In other embodiments, the control member 50 and/or other components of the support structure 22 may be composed of different materials and/or have a different arrangement. For example, the control member 50 may be formed from other suitable shape memory materials (e.g., nickel-titanium (nitinol), wire or tubing besides HHS, shape memory polymers, electro-active polymers) that are pre-formed or pre-shaped into the desired deployed state. Alternatively, the control member 50 may be formed from multiple materials such as a composite of one or more polymers and metals.

[0033] The array of energy delivery elements 24 can include series of separate band electrodes spaced along the support structure 22 and bonded to the tube 42 using an adhesive. Band or tubular electrodes may be used in some embodiments, for example, because they typically have lower power requirements for ablation as compared to disc or flat electrodes. In other embodiments, however, disc or flat electrodes are also suitable. In still another embodiment, electrodes having a spiral or coil shape may be utilized. In some embodiments, the energy delivery elements 24 may be equally spaced apart along the length of the support structure 22. The energy delivery elements 24 may be formed from any suitable metallic material (e.g., gold, platinum, an alloy of platinum and iridium, etc.). In other embodiments, however, the number, arrangement, and/or composition of the energy delivery elements 24 may vary.

[0034] FIG. 4 is an enlarged view of a portion of the catheter 12 of FIG. 3A. Referring to FIGS. 1 and 4 together, each energy delivery element or electrode 24 is electrically connected to the energy source 26 (FIG. 1) by a conductor or bifilar wire 44 extending through a lumen of the tube 42. Each energy delivery element 24 may be welded or otherwise electrically coupled to its energy supply wire 44, and each wire 44 can extend through the tube 42 and elongated shaft 16 (FIG. 1) for the entire length of the shaft such that a proximal end thereof is coupled to the energy source 26 (FIG. 1). As noted above, the tube 42 is configured to fit tightly against the control member 50 and wires 44 to minimize the space between an inner portion of the tube 42 and the components positioned therein to help prevent the formation of wrinkles in the therapeutic assembly 21 during deployment. In some embodiments, the catheter 12 may also include an insulating layer (e.g., a layer of PET or another suitable material) over the control member 50 to further electrically isolate the material (e.g., HHS) of the control member 50 from the wires 44.

[0035] As best seen in FIG. 4, each energy delivery element 24 may include tapered end portions 24a (e.g., fillets) configured to provide an obtuse angle between an outer surface of the tube 42 and an outer surface of the corresponding energy delivery element 24. The smooth transition in angle provided by the tapered end portions 24a is expected to help prevent a guide sheath or loading tool from getting stuck or catching the edges of the energy delivery elements 24 as the guide sheath or loading tool is moved over the length of the therapeutic assembly 21 (FIGS. 3A and 3B) during advancement and retrieval. In other embodiments, the extent of the tapered portions 24a on the energy delivery elements 24 may vary. In some embodiments, the tapered end portions 24a comprise fillets formed from adhesive material at either end of the corresponding energy delivery elements 24. In other embodiments, however, the tapered end portions 24a may be formed from the same material as the tube 42 (e.g., integrally formed with the tube 42 or formed separately and attached to either end of corresponding energy delivery elements 24). Further, the tapered portions 24a are an optional feature that may not be included in some embodiments.

[0036] Referring back to FIGS. 3A and 3B, the therapeutic assembly 21 includes the atraumatic, flexible curved tip 40 at a distal end of the assembly 21. The curved tip 40 is configured to provide a distal opening 41 for the guide wire 66 (FIG. 2) that directs the guide wire away from the wall of the renal artery when the therapeutic assembly 21 is in the pre-set deployed configuration. This feature is expected to facilitate alignment of the helical therapeutic assembly 21 in the renal blood vessel as it expands, while also reducing the risk of injuring the blood vessel wall when the guide wire distal tip is advanced from the opening 41. The curvature of the tip 40 can be varied depending upon the particular sizing/configuration of the therapeutic assembly 21. As best seen in FIG 3B, for example, in the illustrated embodiment the tip 40 is curved such that it is off the pre-set spiral/helical axis defined by the control member 50. In other embodiments, however, the tip 40 may have a different curvature. In some embodiments, the tip 40 may also comprise one or more radiopaque markers 52 and/or one or more sensors (not shown). The tip 40 can be affixed to the distal end of the support structure 22 via adhesive, crimping, over-molding, or other suitable techniques.

[0037] The flexible curved tip 40 can be made from a polymer material (e.g., polyether block amide copolymer sold under the trademark PEBAX), a thermoplastic polyether urethane material (sold under the trademarks ELASTHANE or PELLETHANE), or other suitable materials having the desired properties, including a selected durometer. As noted above, the tip 40 is configured to provide an opening for the guide wire 66, and it is desirable that the tip itself maintain a desired shape/configuration during operation. Accordingly, in some embodiments, one or more additional materials may be added to the tip material to help improve tip shape retention. In one particular embodiment, for example, about 5 to 30 weight percent of siloxane can be blended with the tip material (e.g., the thermoplastic polyether urethane material), and electron beam or gamma irradiation may be used to induce crosslinking of the materials. In other embodiments, the tip 40 may be formed from different material(s) and/or have a different arrangement.

[0038] In operation (and with reference to FIGS. 2, 3A, and 3B), after positioning the therapeutic assembly 21 at the desired location within the renal artery RA of the patient, the therapeutic assembly 21 may be transformed from its delivery state to its deployed state or deployed arrangement. The transformation may be initiated using an arrangement of device components as described herein with respect to the particular embodiments and their various modes of deployment. In one embodiment, for example, the therapeutic assembly 21 may be deployed by retracting the guide wire 66 until a distal tip of the guide wire 66 is generally aligned with the tip 40 of the catheter 12. In some embodiments, the guide wire 66 may have a varying stiffness or flexibility along its length so as to provide increased flexibility distally. When the varying flexible guide wire 66 is partially retracted as described above, the pre-set helical shape of the control member 50 provides a shape-recovery force sufficient to overcome the straightening force provided by the distalmost portion of the guide wire 66 such that the therapeutic assembly 21 can deploy into its helical configuration. Further, because the flexible distal portion of the guide wire 66 remains within the therapeutic assembly 21 in the deployed state, the guide wire 66 can impart additional structural integrity to the helically-shaped portion during treatment. This feature is expected to help mitigate or reduce problems associated with keeping the therapeutic assembly 21 in place during treatment (e.g., help with vasoconstriction).

[0039] In another embodiment, the guide wire 66 may have a stiffness profile that permits the distal portion of the guide wire 66 to remain extended from the opening 41 while still permitting the therapeutic assembly 21 to transform to its deployed configuration. In still other embodiments, the guide wire 66 may be withdrawn completely from the therapeutic assembly 21 (e.g., a distalmost end portion of the guide wire 66 is proximal of the therapeutic assembly 21) to permit the transformation, while a distalmost portion of the guide wire 66 remains within the shaft 16. In yet another embodiment, the guide wire 66 may be withdrawn completely from the shaft 16. In any of the foregoing examples, the clinician can withdraw the guide wire 66 sufficiently to observe transformation of the therapeutic assembly 21 to the deployed configuration and/or until an X-ray image shows that the distal tip of the guide wire 66 is at a desired location relative to the therapeutic assembly 21 (e.g., generally aligned with the tip 40, completely withdrawn from the therapeutic assembly 21, etc.). In some embodiments, the extent of withdrawal for the guide wire 66 can be based, at least in part, on the clinician's judgment with respect to the selected guide wire and the extent of withdrawal necessary to achieve deployment.

[0040] After treatment, the therapeutic assembly 21 may be transformed back to the low-profile delivery configuration by axially advancing the guide wire 66 relative to the therapeutic assembly 21. In one embodiment, for example, the guide wire 66 may be advanced until the distal tip of the guide wire 66 is generally aligned with the tip 40, and the catheter 12 can then be pulled back over the stationary guide wire 66. In other embodiments, however, the distalmost portion of the guide wire 66 may be advanced to different location relative to the therapeutic assembly 21 to achieve transformation of the therapeutic assembly 21 back to low-profile arrangement.

[0041] The embodiments of the catheter systems described above include a procedural guide wire to guide the catheter to the treatment site and also to restrain the therapeutic assembly or treatment section in a low-profile delivery state. In further embodiments, catheter systems configured in accordance with the present technology may further include an external loading tool that can be disposed and retracted over the therapeutic assembly to further assist with transforming the therapeutic assembly between the delivery and deployed configurations.

[0042] FIG. 5, for example, is a partially schematic side view of a loading tool 190 in accordance with an embodiment of the present technology. The loading tool 190 is a tubular structure configured to slidably move along an outer surface of the shaft 16 and the therapeutic assembly 21 (for purposes of illustration, the therapeutic assembly 21 and associated features are shown in broken lines). The loading tool 190 has a size and stiffness suitable for maintaining the therapeutic assembly 21 in the low-profile configuration for backloading of the guide wire 66 (FIG. 2), i.e., insertion of the proximal end of guide wire 66 into the distal opening 41. In the illustrated embodiment, the loading tool 190 can include a tapered portion 192 to help facilitate advancement of the sheath over the therapeutic assembly 21 and the associated energy delivery elements 24. In some embodiments, a distal portion 194 of the loading tool 190 may also include smooth, rounded inner and outer edges 195 to help ease the inner wall of the loading tool over the energy delivery elements 24 during advancement of the loading tool relative to the therapeutic assembly 21. The loading tool 190 may be composed of high-density polyethylene (HDPE) or other suitable materials having a desired strength and lubricity. In still other embodiments, the loading tool 190 may be composed of two or more different materials. In one embodiment, for example, the larger diameter section of the loading tool 190 distal of the tapered portion 192 may be composed of HDPE, while the smaller diameter section of the loading tool 190 proximal of the tapered portion 192 may be composed of linear low-density polyethylene (LLDPE). In still further embodiments, the loading tool 190 may be composed of different materials and/or have a different arrangement.

[0043] In some embodiments, the loading tool 190 may be used in conjunction with the catheter 12 while the catheter 12 is external to the patient before treatment, and then removed from the catheter 12 before the catheter 12 is inserted into the patient. More specifically, as discussed above, the loading tool 190 can be used to maintain the therapeutic assembly 21 in the low-profile configuration while the guide wire is backloaded (moving from a distal end toward a proximal end of the catheter 12). The loading tool 190 can then be removed from the catheter 12, and the therapeutic assembly 21 can be restrained in the delivery configuration with the support of the guide wire. In another embodiment, the loading tool 190 may remain installed on the catheter 12 after backloading of the guide wire, but may be slid down the length of the catheter 12 to a proximal portion 18 of the catheter

12 near the handle 34 (FIG. 1). In this way, the loading tool 190 remains with the catheter 12, but is out of the way during treatment.

[0044] In still other embodiments, however, the loading tool 190 may remain at or near the distal portion 20 (FIG 1) of the catheter 12 during treatment. For example, in one embodiment, a clinician may keep the loading tool 190 at or near the distal portion 20 of the catheter 12 and then insert the loading tool 190 into a hemostasis valve (not shown) connected to a guide catheter (not shown). Depending upon a profile of the loading tool 190 and an inner diameter of the hemostasis valve, the clinician may be able to insert approximately 2 to 4 cm of the loading tool 190 into the hemostasis valve. One advantage of this approach is that the therapeutic assembly 21 (FIGS. 3A and 3B) is further protected as the catheter 12 is advanced through the hemostasis valve, and the clinician is expected to feel little or no friction between the catheter 12 and the hemostasis valve. In other embodiments, however, the loading tool 190 may have a different arrangement relative to the hemostasis valve and/or the other components of the system 10 (FIG. 1) during operation.

III. Pertinent Anatomy and Physiology

[0045] The following discussion provides further details regarding pertinent patient anatomy and physiology. This section is intended to supplement and expand upon the previous discussion regarding the relevant anatomy and physiology, and to provide additional context regarding the disclosed technology and the therapeutic benefits associated with renal neuromodulation. For example, as mentioned previously, several properties of the renal vasculature may inform the design of treatment devices and associated methods for achieving renal neuromodulation, and impose specific design requirements for such devices. Specific design requirements may include accessing the renal artery, ureter, or renal pelvic anatomy, facilitating stable contact between a therapeutic element of a treatment device and a luminal surface or wall, and/or effectively modulating the renal nerves using the therapeutic element.

A. The Sympathetic Nervous System

[0046] The SNS is a branch of the autonomic nervous system along with the enteric nervous system and parasympathetic nervous system. It is always active at a basal level (called sympathetic tone) and becomes more active during times of stress. Like other parts of the nervous system, the sympathetic nervous system operates through a series of interconnected neurons. Sympathetic neurons are frequently considered part of the peripheral nervous system (PNS), although many lie within the central nervous system (CNS). Sympathetic neurons of the spinal cord (which is part of the CNS) communicate with peripheral sympathetic neurons via a series of sympathetic ganglia. Within the ganglia, spinal cord sympathetic neurons join peripheral sympathetic neurons through synapses. Spinal cord sympathetic neurons are therefore called presynaptic (or preganglionic) neurons, while peripheral sympathetic neurons are called postsynaptic (or postganglionic) neurons.

[0047] At synapses within the sympathetic ganglia, preganglionic sympathetic neurons release acetylcholine, a chemical messenger that binds and activates nicotinic acetylcholine receptors on postganglionic neurons. In response to this stimulus, postganglionic neurons principally release noradrenaline (norepinephrine). Prolonged activation may elicit the release of adrenaline from the adrenal medulla.

[0048] Once released, norepinephrine and epinephrine bind adrenergic receptors on peripheral tissues. Binding to adrenergic receptors causes a neuronal and hormonal response. The physiologic manifestations include pupil dilation, increased heart rate, occasional vomiting, and increased blood pressure. Increased sweating is also seen due to binding of cholinergic receptors of the sweat glands.

[0049] The sympathetic nervous system is responsible for up- and down-regulating many homeostatic mechanisms in living organisms. Fibers from the SNS extend through tissues in almost every organ system, providing at least some regulatory function to characteristics as diverse as pupil diameter, gut motility, and urinary output. This response is also known as *sympatho-adrenal response* of the body, as the preganglionic sympathetic fibers that end in the adrenal medulla (but also all other sympathetic fibers) secrete acetylcholine, which activates the secretion of adrenaline (epinephrine) and to a lesser extent noradrenaline (norepinephrine). Therefore, this response that acts primarily on the cardiovascular system is mediated directly via impulses transmitted through the sympathetic nervous system and indirectly via catecholamines secreted from the adrenal medulla.

[0050] Science typically looks at the SNS as an automatic regulation system, that is, one that operates without the intervention of conscious thought. Some evolutionary theorists suggest that the sympathetic nervous system operated in early organisms to maintain survival as the sympathetic nervous system is responsible for priming the body for action. One example of this priming is in the moments before waking, in which sympathetic outflow spontaneously increases in preparation for action.

1. The Sympathetic Chain

[0051] As shown in FIG. 6, the SNS provides a network of nerves that allows the brain to communicate with the body. Sympathetic nerves originate inside the vertebral column, toward the middle of the spinal cord in the intermediolateral cell column (or lateral horn), beginning at the first thoracic segment of the spinal cord and are thought to extend to the second or third lumbar segments. Because its cells begin in the thoracic and lumbar regions of the spinal cord, the SNS is said to have a *thoracolumbar outflow*. Axons of these nerves leave the spinal cord through the anterior rootlet/root. They pass near the spinal (sensory) ganglion, where they enter the anterior rami of the spinal nerves. However, unlike somatic innervation, they quickly separate out through white rami connectors which connect to either the paravertebral (which lie near the vertebral column) or prevertebral (which lie near the aortic bifurcation) ganglia extending alongside the spinal column.

[0052] In order to reach the target organs and glands, the axons should travel long distances in the body, and, to accomplish this, many axons relay their message to a second cell through synaptic transmission. The ends of the axons link across a space, the synapse, to the dendrites of the second cell. The first cell (the presynaptic cell) sends a neurotransmitter across the synaptic cleft where it activates the second cell (the postsynaptic cell). The message is then carried to the final destination.

[0053] In the SNS and other components of the peripheral nervous system, these synapses are made at sites called ganglia. The cell that sends its fiber is called a preganglionic cell, while the cell whose fiber leaves the ganglion is called a postganglionic cell. As mentioned previously, the preganglionic cells of the SNS are located between the first thoracic (T1) segment and third lumbar (L3) segments of the spinal cord. Postganglionic cells have their cell bodies in the ganglia and send their axons to target organs or glands.

[0054] The ganglia include not just the sympathetic trunks but also the cervical ganglia (superior, middle and inferior), which send sympathetic nerve fibers to the head and thorax organs, and the celiac and mesenteric ganglia (which send sympathetic fibers to the gut).

2. Nerves of the Kidneys

[0055] As shown in FIG. 7, the kidney neural system includes the renal plexus, which is intimately associated with the renal artery. The renal plexus is an autonomic plexus that surrounds the renal artery and is embedded within the adventitia of the renal artery. The renal plexus extends along the renal artery until it arrives at the substance of the kidney. Fibers contributing to the renal plexus arise from the celiac ganglion, the superior mesenteric ganglion, the aorticorenal ganglion and the aortic plexus. The renal plexus, also referred to as the renal nerve, is predominantly comprised of sympathetic components. There is no (or at least very minimal) parasympathetic neural activity of the kidney.

[0056] Preganglionic neuronal cell bodies are located in the intermediolateral cell column of the spinal cord. Preganglionic axons pass through the paravertebral ganglia (they do not synapse) to become the lesser splanchnic nerve, the least splanchnic nerve, first lumbar splanchnic nerve, second lumbar splanchnic nerve, and travel to the celiac ganglion, the superior mesenteric ganglion, and the aorticorenal ganglion. Postganglionic neuronal cell bodies exit the celiac ganglion, the superior mesenteric ganglion, and the aorticorenal ganglion to the renal plexus and are distributed to the renal vasculature.

3. Renal Sympathetic Neural Activisty

[0057] Messages travel through the SNS in a bidirectional flow. Efferent messages may trigger changes in different parts of the body simultaneously. For example, the sympathetic nervous system may accelerate heart rate, widen bronchial passages, decrease motility (movement) of the large intestine, constrict blood vessels, increase peristalsis in the esophagus, cause pupil dilation, piloerection (goose bumps) and perspiration (sweating), and raise blood pressure. Afferent messages carry signals from various organs and sensory receptors in the body to other organs and, particularly, the brain.

[0058] Hypertension, heart failure and chronic kidney disease are a few of many disease states that result from chronic activation of the SNS, especially the renal sympathetic nervous system. Chronic activation of the SNS is a maladaptive response that drives the progression of these disease states. Pharmaceutical management of the renin-angiotensin-aldosterone system (RAAS) has been a longstanding, but somewhat ineffective, approach for reducing overactivity of the SNS.

[0059] As mentioned above, the renal sympathetic nervous system has been identified as a major contributor to the complex pathophysiology of hypertension, states of volume overload (such as heart failure), and progressive renal disease, both experimentally and in humans. Studies employing radiotracer dilution methodology to measure overflow of norepinephrine from the kidneys to plasma revealed increased renal norepinephrine (NE) spillover rates in patients with essential hypertension, particularly so in young hypertensive subjects, which in concert with increased NE spillover from the heart, is consistent with the hemodynamic profile typically seen in early hypertension and characterized by an increased heart rate, cardiac output, and renovascular resistance. It is now known that essential hypertension is commonly neurogenic, often accompanied by pronounced sympathetic nervous system overactivity.

[0060] Activation of cardiorenal sympathetic nerve activity is even more pronounced in heart failure, as demonstrated by an exaggerated increase of NE overflow from the heart and the kidneys to plasma in this patient group. In line with this notion is the recent demonstration of a strong negative predictive value of renal sympathetic activation on all-cause mortality and heart transplantation in patients with congestive heart failure, which is independent of overall sympathetic activity, glomerular filtration rate, and left ventricular ejection fraction. These findings support the notion that treatment regimens that are designed to reduce renal sympathetic stimulation have the potential to improve survival in patients with heart failure.

[0061] Both chronic and end stage renal disease are characterized by heightened sympathetic nervous activation. In patients with end stage renal disease, plasma levels of norepinephrine above the median have been demonstrated to be predictive for both all-cause death and death from cardiovascular disease. This is also true for patients suffering from diabetic or contrast nephropathy. There is compelling evidence suggesting that sensory efferent signals originating from the diseased kidneys are major contributors to initiating and sustaining elevated central sympathetic outflow in this patient group; this facilitates the occurrence of the well-known adverse consequences of chronic sympathetic over activity, such as hypertension, left ventricular hypertrophy, ventricular arrhythmias, sudden cardiac death, insulin resistance, diabetes, and metabolic syndrome.

i. Renal Sympathetic Efferent Activity

[0062] Sympathetic nerves to the kidneys terminate in the blood vessels, the juxtaglomerular apparatus and the renal tubules. Stimulation of the renal sympathetic nerves causes increased renin release, increased sodium (Na^+) reabsorption, and a reduction of renal blood flow. These components of the neural regulation of renal function are considerably stimulated in disease states characterized by heightened sympathetic tone and clearly contribute to the rise in blood pressure in hypertensive patients. The reduction of renal blood flow and glomerular filtration rate as a result of renal sympathetic efferent stimulation is likely a cornerstone of the loss of renal function in cardio-renal syndrome, which is renal dysfunction as a progressive complication of chronic heart failure, with a clinical course that typically fluctuates with the patient's clinical status and treatment. Pharmacologic strategies to thwart the consequences of renal efferent sympathetic stimulation include centrally acting sympatholytic drugs, beta blockers (intended to reduce renin release), angiotensin converting enzyme inhibitors and receptor blockers (intended to block the action of angiotensin II and aldosterone activation consequent to renin release) and diuretics (intended to counter the renal sympathetic mediated sodium and water retention). However, the current pharmacologic strategies have significant limitations including limited efficacy, compliance issues, side effects and others.

ii. Renal Sensory Afferent Nerve Activity

[0063] The kidneys communicate with integral structures in the central nervous system via renal sensory efferent nerves. Several forms of "renal injury" may induce activation of sensory efferent signals. For example, renal ischemia, reduction in stroke volume or renal blood flow, or an abundance of adenosine may trigger activation of afferent neural communication. As shown in FIGS. 8A and 8B, this afferent communication might be from the kidney to the brain or might be from one kidney to the other kidney (via the central nervous system). These afferent signals are centrally integrated and may result in increased sympathetic outflow. This sympathetic drive is directed towards the kidneys, thereby activating the RAAS and inducing increased renin secretion, sodium retention, fluid volume retention, and vasoconstriction. Central sympathetic over activity also impacts other organs and bodily structures having sympathetic nerves such as the heart and the peripheral vasculature, resulting in the described adverse effects of sympathetic activation, several aspects of which also contribute to the rise in blood pressure.

[0064] The physiology therefore suggests that (i) modulation of tissue with efferent sympathetic nerves will reduce inappropriate renin release, sodium retention, and reduction of renal blood flow, and that (ii) modulation of tissue with afferent sensory nerves will reduce the systemic contribution to hypertension and other disease states associated with increased central sympathetic tone through its direct effect on the posterior hypothalamus as well as the contralateral kidney. In addition to the central hypotensive effects of afferent renal neuromodulation, a desirable reduction of central sympathetic outflow to various other organs such as the heart and the vasculature is anticipated.

B. Additional Clinical Benefits of Renal Neuromodulation

[0065] As provided above, renal neuromodulation is likely to be valuable in the treatment of several clinical conditions characterized by increased overall and particularly renal sympathetic activity such as hypertension, metabolic syndrome, insulin resistance, diabetes, left ventricular hypertrophy, chronic end stage renal disease, inappropriate fluid retention in heart failure, cardio-renal syndrome, and sudden death. Since the reduction of afferent neural signals contributes to the systemic reduction of sympathetic tone/drive, renal neuromodulation might also be useful in treating other conditions associated with systemic sympathetic hyperactivity. Accordingly, renal neuromodulation may also benefit other organs and bodily structures having sympathetic nerves, including those identified in FIG. 6.

C. Achieving Intravascular Access to the Renal Artery

[0066] In accordance with the present technology, neuromodulation of a left and/or right renal plexus RP, which is intimately associated with a left and/or right renal artery, may be achieved through intravascular access. As FIG. 9A shows, blood moved by contractions of the heart is conveyed from the left ventricle of the heart by the aorta. The aorta descends through the thorax and branches into the left and right renal arteries. Below the renal arteries, the aorta bifurcates at the left and right iliac arteries. The left and right iliac arteries descend, respectively, through the left and right legs and join the left and right femoral arteries.

[0067] As FIG. 9B shows, the blood collects in veins and returns to the heart, through the femoral veins into the iliac veins and into the inferior vena cava. The inferior vena cava branches into the left and right renal veins. Above the renal veins, the inferior vena cava ascends to convey blood into the right atrium of the heart. From the right atrium, the blood is pumped through the right ventricle into the lungs, where it is oxygenated. From the lungs, the oxygenated blood is conveyed into the left atrium. From the left atrium, the oxygenated blood is conveyed by the left ventricle back to the aorta.

[0068] As provided herein, the femoral artery may be accessed and cannulated at the base of the femoral triangle just inferior to the midpoint of the inguinal ligament. A catheter may be inserted percutaneously into the femoral artery through this access site, passed through the iliac artery and aorta, and placed into either the left or right renal artery. This comprises an intravascular path that offers minimally invasive access to a respective renal artery and/or other renal blood vessels.

[0069] The wrist, upper arm, and shoulder region provide other locations for introduction of catheters into the arterial system. For example, catheterization of either the radial, brachial, or axillary artery may be utilized in select cases. Catheters introduced via these access points may be passed through the subclavian artery on the left side (or via the subclavian and brachiocephalic arteries on the right side), through the aortic arch, down the descending aorta and into the renal arteries using standard angiographic technique.

D. Properties and Characteristics of the Renal Vasculature

[0070] Since neuromodulation of a left and/or right renal plexus may be achieved in accordance with the present technology through intravascular access, properties and characteristics of the renal vasculature may impose constraints upon and/or inform the design of apparatus, systems, and methods for achieving such renal neuromodulation. Some of these properties and characteristics may vary across the patient population and/or within a specific patient across time, as well as in response to disease states, such as hypertension, chronic kidney disease, vascular disease, end-stage renal disease, insulin resistance, diabetes, metabolic syndrome, etc. These properties and characteristics, as explained herein, may have bearing on the efficacy of the procedure and the specific design of the intravascular device. Properties of interest may include, for example, material/mechanical, spatial, fluid dynamic/hemodynamic and/or thermodynamic properties.

[0071] As discussed previously, a catheter may be advanced percutaneously into either the left or right renal artery via a minimally invasive intravascular path. However, minimally invasive renal arterial access may be challenging, for example, because as compared to some other arteries that are routinely accessed using catheters, the renal arteries are often extremely tortuous, may be of relatively small diameter, and/or may be of relatively short length. Furthermore, renal arterial atherosclerosis is common in many patients, particularly those with cardiovascular disease. Renal arterial anatomy also may vary significantly from patient to patient, which further complicates minimally invasive access. Significant interpatient variation may be seen, for example, in relative tortuosity, diameter, length, and/or atherosclerotic plaque burden, as well as in the take-off angle at which a renal artery branches from the aorta. Apparatus, systems and methods for achieving renal neuromodulation via intravascular access should account for these and other aspects of renal arterial anatomy and its variation across the patient population when minimally invasively accessing a renal artery.

[0072] In addition to complicating renal arterial access, specifics of the renal anatomy also complicate establishment of stable contact between neuromodulatory apparatus and a luminal surface or wall of a renal artery. When the neuromodulatory apparatus includes an energy delivery element, such as an electrode, consistent positioning and appropriate contact force applied by the energy delivery element to the vessel wall can be important for predictability. However, navigation typically is impeded by the tight space within a renal artery, as well as tortuosity of the artery. Furthermore, establishing consistent contact can be complicated by patient movement, respiration, and/or the cardiac cycle. These factors, for example, may cause significant movement of the renal artery relative to the aorta, and the cardiac cycle may transiently distend the renal artery (i.e., cause the wall of the artery to pulse).

[0073] After accessing a renal artery and facilitating stable contact between neuromodulatory apparatus and a luminal surface of the artery, nerves in and around the adventitia of the artery can be safely modulated via the neuromodulatory apparatus. Effectively applying thermal treatment from within a renal artery is non-trivial given the potential clinical complications associated with such treatment. For example, the intima and media of the renal artery are highly vulnerable to thermal injury. As discussed in greater detail below, the intima-media thickness separating the vessel lumen from its adventitia means that target renal nerves may be multiple millimeters distant from the luminal surface of the artery. Sufficient energy can be delivered to the target renal nerves to modulate the target renal nerves without excessively cooling or heating the vessel wall to the extent that the wall is frozen, desiccated, or otherwise potentially affected to an undesirable extent. A potential clinical complication associated with excessive heating is thrombus formation from coagulating blood flowing through the artery. Accordingly, the complex fluid mechanics and thermodynamic conditions present in the renal artery during treatment, particularly those that may impact heat transfer dynamics at the treatment site, may be important in applying energy from within the renal artery.

[0074] The neuromodulatory apparatus can be configured to allow for adjustable positioning and repositioning of the energy delivery element within the renal artery since location of treatment may also impact clinical efficacy. For example, it may be tempting to apply a full circumferential treatment from within the renal artery given that the renal nerves may be spaced circumferentially around a renal artery. In some situations, full-circle lesion likely resulting from a continuous circumferential treatment may be potentially related to renal artery stenosis. Therefore, the formation of more complex lesions along a longitudinal dimension of the renal artery and/or repositioning of the neuromodulatory apparatus to multiple treatment locations may be desirable. It should be noted, however, that a benefit of creating a circumferential ablation may outweigh the potential of renal artery stenosis or the risk may be mitigated with certain embodiments or in certain patients and creating a circumferential ablation could be a goal. Additionally, variable positioning and repositioning of the neuromodulatory apparatus may prove to be useful in circumstances where the renal artery is particularly tortuous or where there are proximal branch vessels off the renal artery main vessel, making treatment in certain locations challenging.

[0075] Blood flow through a renal artery may be temporarily occluded for a short time with minimal or no complications. However, occlusion for a significant amount of time can be avoided in some cases to reduce the likelihood of injury to the kidney such as ischemia. It could be beneficial to avoid occlusion all together or, if occlusion is beneficial to the embodiment, to limit the duration of occlusion, for example to 2-5 minutes.

[0076] Based on the above described challenges of (1) renal artery intervention, (2) consistent and stable placement of the treatment element against the vessel wall, (3) effective application of treatment across the vessel wall, (4) positioning and potentially repositioning the treatment apparatus to allow for multiple treatment locations, and (5) avoiding or limiting duration of blood flow occlusion, various independent and dependent properties of the renal vasculature that may be of interest include, for example, (a) vessel diameter, vessel length, intima-media thickness, coefficient of friction, and tortuosity; (b) distensibility, stiffness and modulus of elasticity of the vessel wall; (c) peak systolic, end-diastolic blood flow velocity, as well as the mean systolic-diastolic peak blood flow velocity, and mean/max volumetric blood flow rate; (d) specific heat capacity of blood and/or of the vessel wall, thermal conductivity of blood and/or of the vessel wall, and/or thermal convectivity of blood flow past a vessel wall treatment site and/or radiative heat transfer; (e) renal artery motion relative to the aorta induced by respiration, patient movement, and/or blood flow pulsatility; and (f) the take-off angle of a renal artery relative to the aorta. These properties will be discussed in greater detail with respect to the renal arteries. However, depending on the apparatus, systems, and methods utilized to achieve renal neuromodulation, such properties of the renal arteries also may guide and/or constrain design characteristics.

[0077] As noted above, an apparatus positioned within a renal artery can conform to the geometry of the artery. Renal artery vessel diameter, D_{RA}, typically is in a range of about 2-10 mm, with most of the patient population having a D_{RA} of about 4 mm to about 8 mm and an average of about 6 mm. Renal artery vessel length, L_{RA}, between its ostium at the aorta/renal artery juncture and its distal branchings, generally is in a range of about 5-70 mm, and a significant portion of the patient population is in a range of about 20-50 mm. Since the target renal plexus is embedded within the adventitia of the renal artery, the composite Intima-Media Thickness, IMT, (i.e., the radial outward distance from the artery's luminal surface to the adventitia containing target neural structures) also is notable and generally is in a range of about 0.5-2.5 mm, with an average of about 1.5 mm. Although a certain depth of treatment can be important to reach the target neural fibers, the treatment can be prevented from becoming too deep (e.g., > 5 mm from inner wall of the renal artery) to avoid non-target tissue and anatomical structures such as the renal vein.

[0078] An additional property of the renal artery that may be of interest is the degree of renal motion relative to the aorta, induced by respiration and/or blood flow pulsatility. A patient's kidney, which located at the distal end of the renal artery, may move as much as 4 inches cranially with respiratory excursion. This may impart significant motion to the renal artery connecting the aorta and the kidney, thereby requiring from the neuromodulatory apparatus a unique balance of stiffness and flexibility to maintain contact between the thermal treatment element and the vessel wall during cycles of respiration. Furthermore, the take-off angle between the renal artery and the aorta may vary significantly between patients, and also may vary dynamically within a patient, e.g., due to kidney motion. The take-off angle generally may be in a range of about 30°-135°.

IV. Further Examples

[0079] The following examples are illustrative of several embodiments of the present technology:

1. A catheter apparatus, comprising:

   an elongated tubular shaft having a proximal portion and a distal portion; and
   a therapeutic assembly disposed at the distal portion of the elongated shaft and adapted to be located at a target location within a renal artery of a human patient, the therapeutic assembly including a support structure comprising- a control member comprising a pre-formed helical shape, wherein the control

      member is a tubular structure having a lumen therethrough and is composed of a nitinol multifilar stranded wire; and

a plurality of energy delivery elements carried by the support structure,
wherein the elongated tubular shaft and the therapeutic assembly together define therethrough a guide wire lumen configured to slidably receive a medical guide wire, and
wherein axial movement of the guide wire relative to the therapeutic assembly transforms the support structure between (a) a low-profile delivery configuration and (b) a deployed configuration tending to assume the pre-formed helical shape of the control member.

2. The catheter apparatus of example 1 wherein the therapeutic assembly is configured to transform between the low-profile delivery configuration and the deployed configuration while at least a distal portion of the guide wire remains in the guide wire lumen of the therapeutic assembly.

3. The catheter apparatus of example 2 wherein the support structure comprises a shape-recovery force sufficient to overcome a straightening force provided by a distal region of the guide wire to transform the therapeutic assembly to the deployed configuration when a distalmost tip of the guide wire is generally aligned with a distal tip of the therapeutic assembly.

4. The catheter apparatus of example 1 wherein:

the support structure comprises a shape-recovery force insufficient to overcome a straightening force provided by a distal region of the guide wire when the guide wire is within the guide wire lumen of the therapeutic assembly; and
the therapeutic assembly is configured to transform to the deployed configuration when a distalmost portion of the guide wire is withdrawn though the guide wire lumen to a point proximal of the therapeutic assembly.

5. The catheter apparatus of any one of examples 1 to 4 wherein a distal portion of the therapeutic assembly further comprises a flexible curved tip configured to provide an opening for the guide wire and, in the deployed configuration, to direct the guide wire away from a wall of the renal artery.

6. The catheter apparatus of example 5 wherein the flexible curved tip is composed of polyether block amide copolymer.

7. The catheter apparatus of example 5 wherein the flexible curved tip is composed of a thermoplastic polyether urethane material.

8. The catheter apparatus of example 7 wherein the flexible curved tip is composed of about 5 to 30 weight percent of siloxane blended with the thermoplastic polyether urethane material.

9. The catheter apparatus of any one of examples 1 to 8 wherein, in the deployed configuration, the energy delivery elements carried by the support structure are spaced apart from each other along a longitudinal axis of the renal artery and are configured to maintain apposition with a wall of the renal artery.

10. The catheter apparatus of any one of examples 1 to 9 wherein the energy delivery elements comprise a series of band electrodes.

11. The catheter apparatus of example 10 wherein at least one of the band electrodes comprises tapered end portions, and wherein the tapered end portions are configured to provide an obtuse angle between an outer surface of the support structure and an outer surface of the at least one band electrode.

12. The catheter apparatus of any one of examples 1 to 11 wherein the therapeutic assembly comprises four energy delivery elements.

13. The catheter apparatus of any one of examples 1 to 12, further comprising a retractable loading tool surrounding and restraining at least a longitudinal portion of the therapeutic assembly in the low-profile delivery configuration.

14. The catheter apparatus of example 13 wherein the loading tool comprises a distal end portion having rounded edges.

15. A renal neuromodulation system for treatment of a human patient, the system comprising:

an elongate shaft having a proximal end and a distal end, wherein the distal end of the shaft is configured for intravascular delivery over a procedural guide wire to a renal artery of the patient;
a pre-shaped tubular spiral structure disposed at or proximate to the distal end of the elongate shaft, wherein the spiral structure is configured to transform between an unexpanded configuration and an expanded configuration that tends to assume the shape of the pre-shaped spiral structure, and wherein the spiral structure is composed, at least in part, of multifilar stranded nitinol wire; and
a plurality of electrodes associated with the spiral structure,
wherein the elongate shaft and the spiral structure together define a guide wire lumen there-

through, and wherein-

the guide wire lumen is configured to slidably receive the procedural guide wire to locate the spiral structure at a target treatment site within a renal blood vessel of the patient and to restrain the spiral structure in the unexpanded configuration, and wherein

proximal movement of the procedural guide wire through the guide wire lumen relative to the spiral structure such that a distal end portion of the guide wire is at least partially within the guide wire lumen transforms the spiral structure to the expanded configuration.

16. The system of example 15 wherein the procedural guide wire comprises a distal portion having varying flexibility, and further wherein at least a region of the distal portion of the guide wire is configured to remain within the portion of the guide wire lumen defined by the spiral structure when the spiral structure is in the expanded configuration.

17. The system of example 15 or example 16, further comprising a flexible tube covering and in intimate contact with the spiral structure.

18. The system of example 17 wherein the plurality of electrodes are bonded to the flexible tube using an adhesive material.

19. The system of any one of examples 15 to 18 wherein the plurality of electrodes are composed of gold.

20. The system of any one of examples 15 to 19 wherein the plurality of electrodes are individually connectable to an energy source external to the patient, and wherein the energy source is capable of individually controlling the energy delivered to each electrode during therapy.

21. A method of performing renal neuromodulation, the method comprising:

intravascularly delivering a renal neuromodulation catheter in a low-profile delivery configuration over a guide wire to a target treatment site within a renal blood vessel of a human patient and at least proximate to a renal nerve of the patient, wherein the renal neuromodulation catheter comprises- an elongated shaft; and

a multi-electrode array disposed at a distal portion of the shaft and composed, at least in part, of a tubular structure formed of multifilar nitinol wire;

withdrawing the guide wire in a proximal direction until the catheter transforms from the low-profile delivery configuration to a deployed configuration wherein the tubular structure has a radially expanded, generally spiral shape configured to contact the wall of the renal blood vessel and to allow blood to flow through the vessel; and

selectively delivering energy to one or more electrodes of the multi-electrode array to inhibit neural communication along the renal nerve.

22. The method of example 21 wherein selectively delivering energy to one or more electrodes of the multi-electrode array comprises producing a plurality of lesions in a desired pattern along the renal blood vessel.

23. The method of example 21 or example 22 wherein the individual electrodes of the multi-electrode array are spaced sufficiently apart such that the lesions do not overlap.

24. The method of any one of examples 21 to 23, further comprising attaching an external ground to an exterior of the patient, and wherein selectively delivering energy to one or more electrodes further comprises delivering an electric field in a monopolar fashion between each of the electrodes and the external ground.

25. The method of any one of examples 21 to 23 wherein selectively delivering energy comprises selectively delivering an electric field in a bipolar fashion between the electrodes of the multi-electrode array.

26. The method of any one of examples 21 to 25 wherein withdrawing the guide wire in a proximal direction until the therapeutic assembly transforms comprises only partially withdrawing the guide wire from the therapeutic assembly such that at least a portion of the guide wire remains in the therapeutic assembly after the therapeutic assembly transforms to the deployed configuration.

27. The method of any one of examples 21 to 25 wherein withdrawing the guide wire in a proximal direction until the therapeutic assembly transforms comprises completely withdrawing the guide wire from the therapeutic assembly such that a distalmost portion of the guide wire is withdrawn to a point proximal of the therapeutic assembly.

28. The method of any one of examples 21 to 27 wherein the target treatment site comprises a first target treatment site, and wherein the method further comprises:

advancing the guide wire in a distal direction after selectively delivering energy to the one or more electrodes of the multi-electrode array to

transform the multi-electrode array from the deployed configuration back to the low-profile delivery configuration;
repositioning the catheter at a second target treatment site different than the first treatment site;
withdrawing the guide wire in a proximal direction to again transform the therapeutic assembly from the delivery configuration to the deployed configuration; and
selectively delivering energy to one or more electrodes of the multi-electrode array positioned at the second target treatment site.

V. Conclusion

[0080] The above detailed descriptions of embodiments of the technology are not intended to be exhaustive or to limit the technology to the precise form disclosed above. Although specific embodiments of, and examples for, the technology are described above for illustrative purposes, various equivalent modifications are possible within the scope of the technology, as those skilled in the relevant art will recognize. For example, while steps are presented in a given order, alternative embodiments may perform steps in a different order. The various embodiments described herein may also be combined to provide further embodiments.

[0081] From the foregoing, it will be appreciated that specific embodiments of the technology have been described herein for purposes of illustration, but well-known structures and functions have not been shown or described in detail to avoid unnecessarily obscuring the description of the embodiments of the technology. Where the context permits, singular or plural terms may also include the plural or singular term, respectively.

[0082] Moreover, unless the word "or" is expressly limited to mean only a single item exclusive from the other items in reference to a list of two or more items, then the use of "or" in such a list is to be interpreted as including (a) any single item in the list, (b) all of the items in the list, or (c) any combination of the items in the list. Additionally, the term "comprising" is used throughout to mean including at least the recited feature(s) such that any greater number of the same feature and/or additional types of other features are not precluded. It will also be appreciated that specific embodiments have been described herein for purposes of illustration, but that various modifications may be made without deviating from the technology. Further, while advantages associated with certain embodiments of the technology have been described in the context of those embodiments, other embodiments may also exhibit such advantages, and not all embodiments need necessarily exhibit such advantages to fall within the scope of the technology. Accordingly, the disclosure and associated technology can encompass other embodiments not expressly shown or described herein.

[0083] Further disclosed herein is the subject-matter of the following clauses:

1. A catheter apparatus, comprising:

an elongated tubular shaft having a proximal portion and a distal portion; and a therapeutic assembly disposed at the distal portion of the elongated shaft and adapted to be located at a target location within a renal artery of a human patient, the therapeutic assembly including a support structure comprising a control member comprising a pre-formed helical shape, wherein the control member is a tubular structure having a lumen therethrough and is composed of a nitinol multifllar stranded wire; and a plurality of energy delivery elements carried by the support structure, wherein the elongated tubular shaft and the therapeutic assembly together define therethrough a guide wire lumen configured to slidably receive a medical guide wire, and wherein axial movement of the guide wire relative to the therapeutic assembly transforms the support structure between (a) a low-profile delivery configuration and (b) a deployed configuration tending to assume the preformed helical shape of the control member.

2. The catheter apparatus of clause 1 wherein the therapeutic assembly is configured to transform between the low-profile delivery configuration and the deployed configuration while at least a distal portion of the guide wire remains in the guide wire lumen of the therapeutic assembly.

3. The catheter apparatus of clause 2 wherein the support structure comprises a shape-recovery force sufficient to overcome a straightening force provided by a distal region of the guide wire to transform the therapeutic assembly to the deployed configuration when a distalmost tip of the guide wire is generally aligned with a distal tip of the therapeutic assembly.

4. The catheter apparatus of clause 1 wherein: the support structure comprises a shape-recovery force insufficient to overcome a straightening force provided by a distal region of the guide wire when the guide wire is within the guide wire lumen of the therapeutic assembly; and the therapeutic assembly is configured to transform to the deployed configuration when a distalmost portion of the guide wire is withdrawn though the guide wire lumen to a point proximal of the therapeutic assembly.

5. The catheter apparatus of clause 1 wherein a distal portion of the therapeutic assembly further comprises a flexible curved tip configured to provide an opening for the guide wire and, in the deployed configu-

ration, to direct the guide wire away from a wall of the renal artery.

6. The catheter apparatus of clause 5 wherein the flexible curved tip is composed of polyether block amide copolymer.

7. The catheter apparatus of clause 5 wherein the flexible curved tip is composed of a thermoplastic polyether urethane material.

8. The catheter apparatus of clause 7 wherein the flexible curved tip is composed of about 5 to 30 weight percent of siloxane blended with the thermoplastic polyether urethane material.

9. The catheter apparatus of clause 1 wherein, in the deployed configuration, the energy delivery elements carried by the support structure are spaced apart from each other along a longitudinal axis of the renal artery and are configured to maintain apposition with a wall of the renal artery.

10. The catheter apparatus of clause 1 wherein the energy deliver}' elements comprise a series of band electrodes.

11. The catheter apparatus of clause 10 wherein at least one of the band electrodes comprises tapered end portions, and wherein the tapered end portions are configured to provide an obtuse angle between an outer surface of the support structure and an outer surface of the at least one band electrode.

12. The catheter apparatus of clause 1 wherein the therapeutic assembly comprises four energy delivery elements.

13. The catheter apparatus of clause 1, further comprising a retractable loading tool surrounding and restraining at least a longitudinal portion of the therapeutic assembly in the low-profile delivery configuration.

14. The catheter apparatus of clause 13 wherein the loading tool comprises a distal end portion having rounded edges.

15. A renal neuromodulation system for treatment of a human patient, the system comprising: an elongate shaft having a proximal end and a distal end, wherein the distal end of the shaft is configured for intravascular delivery over a procedural guide wire to a renal artery of the patient; a pre-shaped tubular spiral structure disposed at or proximate to the distal end of the elongate shaft, wherein the spiral structure is configured to transform between an unexpanded configuration and an expanded configuration that tends to assume the shape of the pre-shaped spiral structure, and wherein the spiral structure is composed, at least in part, of multifilar stranded nitinol wire; and a plurality of electrodes associated with the spiral structure, wherein the elongate shaft and the spiral structure together define a guide wire lumen therethrough, and wherein the guide wire lumen is configured to slidably receive the procedural guide wire to locate the spiral structure at a target treatment site within a renal blood vessel of the patient and to restrain the spiral structure in the unexpanded configuration, and wherein proximal movement of the procedural guide wire through the guide wire lumen relative to the spiral structure such that a distal end portion of the guide wire is at least partially within the guide wire lumen transforms the spiral structure to the expanded configuration.

16. The system of clause 15 wherein the procedural guide wire comprises a distal portion having varying flexibility therealong, and further wherein at least a region of the distal portion of the guide wire is configured to remain within the portion of the guide wire lumen defined by the spiral structure when the spiral structure is in the expanded configuration.

17. The system of clause 15, further comprising a flexible tube covering and in intimate contact with the spiral structure.

18. The system of clause 17 wherein the plurality of electrodes are bonded to the flexible tube using an adhesive material.

19. The system of clause 15 wherein the plurality of electrodes are composed of gold.

20. The system of clause 15 wherein the plurality of electrodes are individually connectable to an energy source external to the patient, and wherein the energy source is capable of individually controlling the energy delivered to each electrode during therapy.

21. A method of performing renal neuromodulation, the method comprising;
intravascularly delivering a renal neuromodulation catheter in a low-profile delivery configuration over a guide wire to a target treatment site within a renal blood vessel of a human patient and at least proximate to a renal nerve of the patient, wherein the renal neuromodulation catheter comprises an elongated shaft; and a multi-electrode array disposed at a distal portion of the shaft and composed, at least in part, of a tubular structure formed of multifilar nitinol wire; withdrawing the guide wire in a proximal direction until the catheter transforms from the low-profile delivery configuration to a deployed configuration wherein the tubular structure has a radially expand-

ed, generally spiral shape configured to contact the wall of the renal blood vessel and to allow blood to flow through the vessel; and selectively delivering energy to one or more electrodes of the multi-electrode array to inhibit neural communication along the renal nerve.

22. The method of clause 21 wherein selectively delivering energy to one or more electrodes of the multi-electrode array comprises producing a plurality of lesions in a desired pattern along the renal blood vessel.

23. The method of clause 22 wherein the individual electrodes of the multi-electrode array are spaced sufficiently apart such that the lesions do not overlap.

24. The method of clause 21, further comprising attaching an external ground to an exterior of the patient, and wherein selectively delivering energy to one or more electrodes further comprises delivering an electric field in a monopolar fashion between each of the electrodes and the external ground.

25. The method of clause 21 wherein selectively delivering energy comprises selectively delivering an electric field in a bipolar fashion between the electrodes of the multi-electrode array.

26. The method of clause 21 wherein withdrawing the guide wire in a proximal direction until the therapeutic assembly transforms comprises only partially withdrawing the guide wire from the therapeutic assembly such that at least a portion of the guide wire remains in the therapeutic assembly after the therapeutic assembly transforms to the deployed configuration.

27. The method of clause 21 wherein withdrawing the guide wire in a proximal direction until the therapeutic assembly transforms comprises completely withdrawing the guide wire from the therapeutic assembly such that a distalmost portion of the guide wire is withdrawn to a point proximal of the therapeutic assembly.

28. The method of clause 21 wherein the target treatment site comprises a first target treatment site, and wherein the method further comprises: advancing the guide wire in a distal direction after selectively delivering energy to the one or more electrodes of the multi-electrode array to transform the multi- electrode array from the deployed configuration back to the low-profile delivery configuration; repositioning the catheter at a second target treatment site different than the first treatment site; withdrawing the guide wire in a proximal direction to again transform the therapeutic assembly from the delivery configuration to the deployed configuration; and selectively delivering energy to one or more electrodes of the multi-electrode array positioned at the second target treatment site.

Claims

1. A renal neuromodulation system for treatment of a human patient, the system comprising:

a procedural guidewire wire,
an elongate shaft having a proximal end and a distal end, wherein the distal end of the shaft is configured for intravascular delivery over the procedural guide wire to a renal artery of the patient;
a pre-shaped tubular spiral structure disposed at or proximate to the distal end of the elongate shaft, wherein the spiral structure is configured to transform between an unexpanded configuration and an expanded configuration that tends to assume the shape of the pre-shaped spiral structure, and wherein the spiral structure is composed, at least in part, of multifilar stranded nitinol wire; and
a plurality of electrodes associated with the spiral structure,
wherein the elongate shaft and the spiral structure together define a guide wire lumen therethrough, and wherein
the guide wire lumen is configured to slidably receive the procedural guide wire to locate the spiral structure at a target treatment site within a renal blood vessel of the patient and to restrain the spiral structure in the unexpanded configuration, and wherein proximal movement of the procedural guide wire through the guide wire lumen relative to the spiral structure such that a distal end portion of the guide wire is at least partially within the guide wire lumen transforms the spiral structure to the expanded configuration,
wherein the procedural guide wire is **characterized in that** it comprises a distal portion having varying flexibility.

2. The system of claim 1, wherein at least a region of the distal portion of the guide wire is configured to remain within the portion of the guide wire lumen defined by the spiral structure when the spiral structure is in the expanded configuration, and/or wherein the guide wire is configured to be withdrawn completely from the spiral structure, and/or wherein the guidewire is configured for being withdrawn completely from the shaft.

3. The system of claim 1 or claim 2, further comprising a flexible tube covering and in intimate contact with the spiral structure.

4. The system of claim 3 wherein the plurality of electrodes are bonded to the flexible tube using an adhesive material.

5. The system of any one of claims 1 to 4 wherein the plurality of electrodes are composed of gold.

6. The system of any one of claims 1 to 4 wherein the plurality of electrodes are individually connectable to an energy source external to the patient, and wherein the energy source is capable of individually controlling the energy delivered to each electrode during therapy.

7. The system of any one of claims 1 to 6 wherein, in the expanded configuration, the electrodes associated with the spiral structure are spaced apart from each other along a longitudinal axis of the renal artery and are configured to maintain in apposition with a wall of the renal artery.

8. The system of any one of claims 1 to 7 wherein the electrodes comprise a series of band electrodes.

9. The system of claim 8 wherein at least one of the band electrodes comprises tapered end portions, and wherein the tapered end portions are configured to provide an obtuse angle between an outer surface of the spiral structure and an outer surface of the at least one band electrode.

10. The system of any one of claims 1 to 9 wherein the spiral structure comprises four electrodes.

11. The system of any one of claims 1 to 10, further comprising a retractable loading tool surrounding and restraining at least a longitudinal portion of the spiral structure in the low-profile delivery configuration.

12. The system of claim 11 wherein the loading tool comprises a distal end portion having rounded edges.

13. The system of any one of claims 1 to 12, further comprising an energy source such as an RF energy generator.

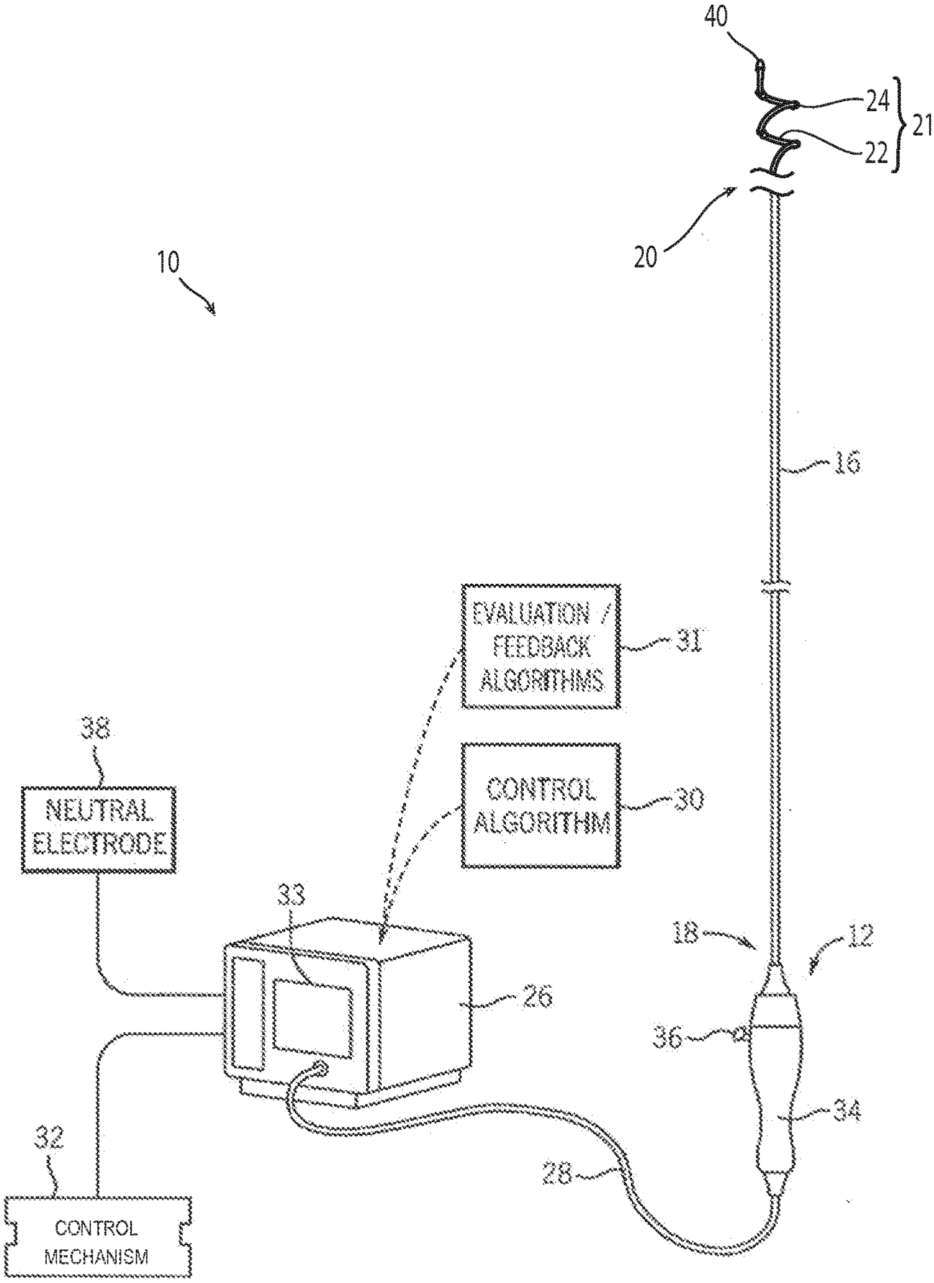
40
24
21
22
20
10
16
EVALUATION / FEEDBACK ALGORITHMS
31
CONTROL ALGORITHM
30
38
NEUTRAL ELECTRODE
33
18
12
26
36
34
32
28
CONTROL MECHANISM

FIG. 1

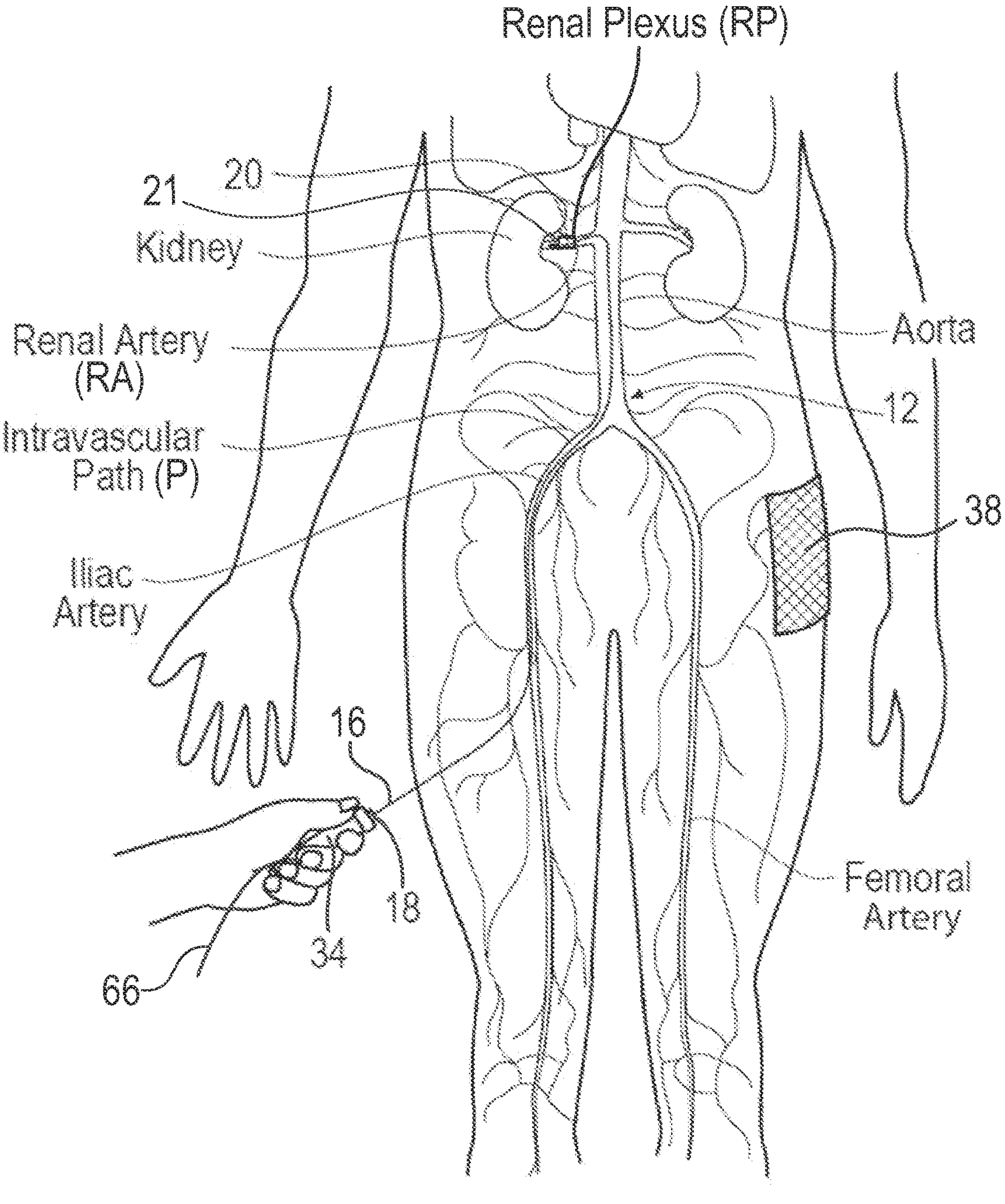
Renal Plexus (RP)
20
21
Kidney
Renal Artery (RA)
Intravascular Path (P)
Iliac Artery
Aorta
12
38
16
18
34
66
Femoral Artery

FIG. 2

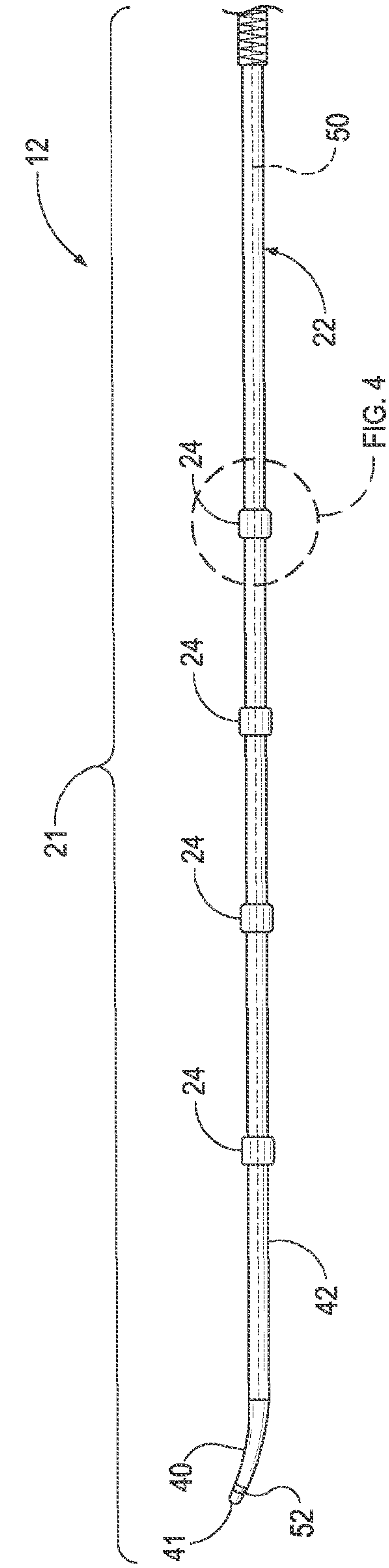

FIG. 3A

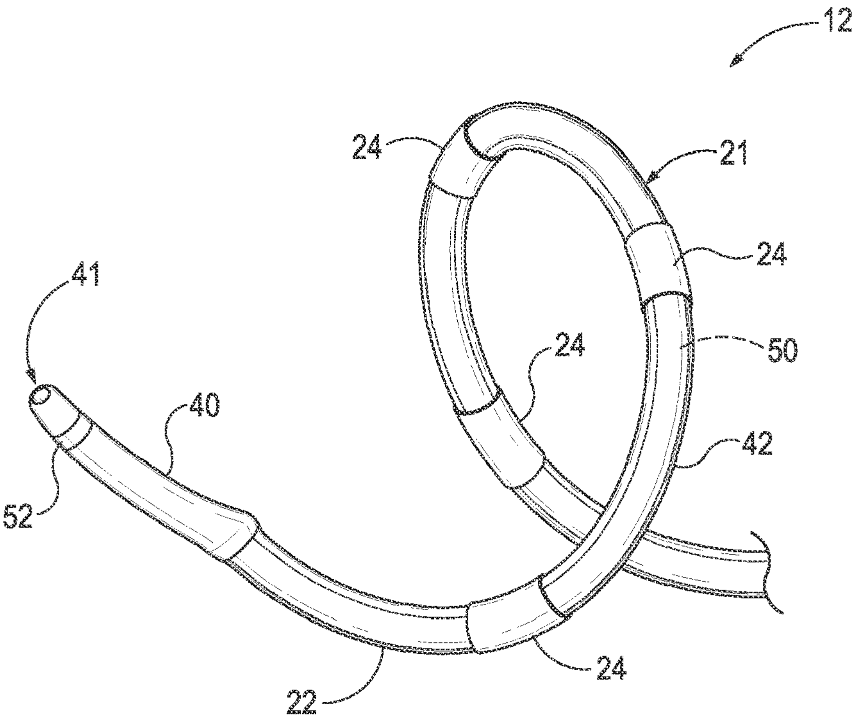

FIG. 3B

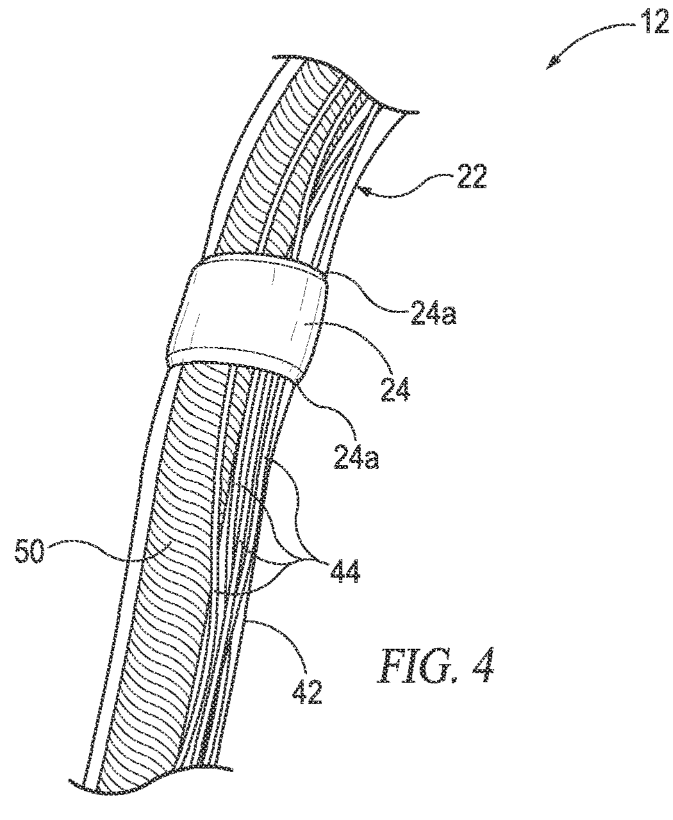

FIG. 4

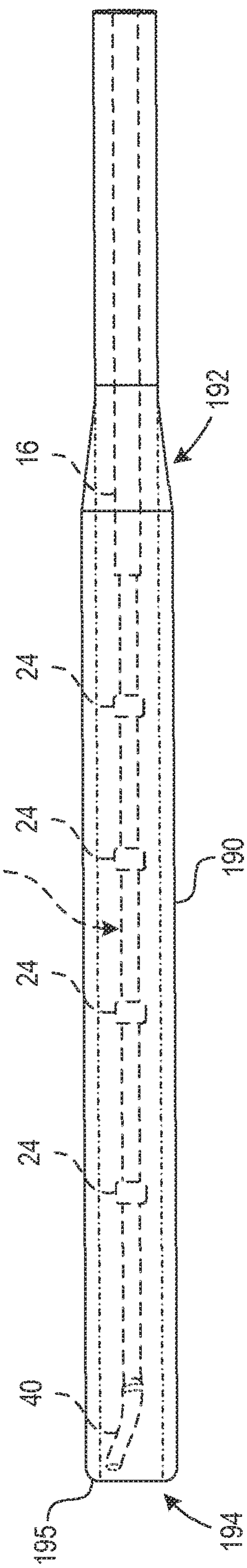

FIG. 5

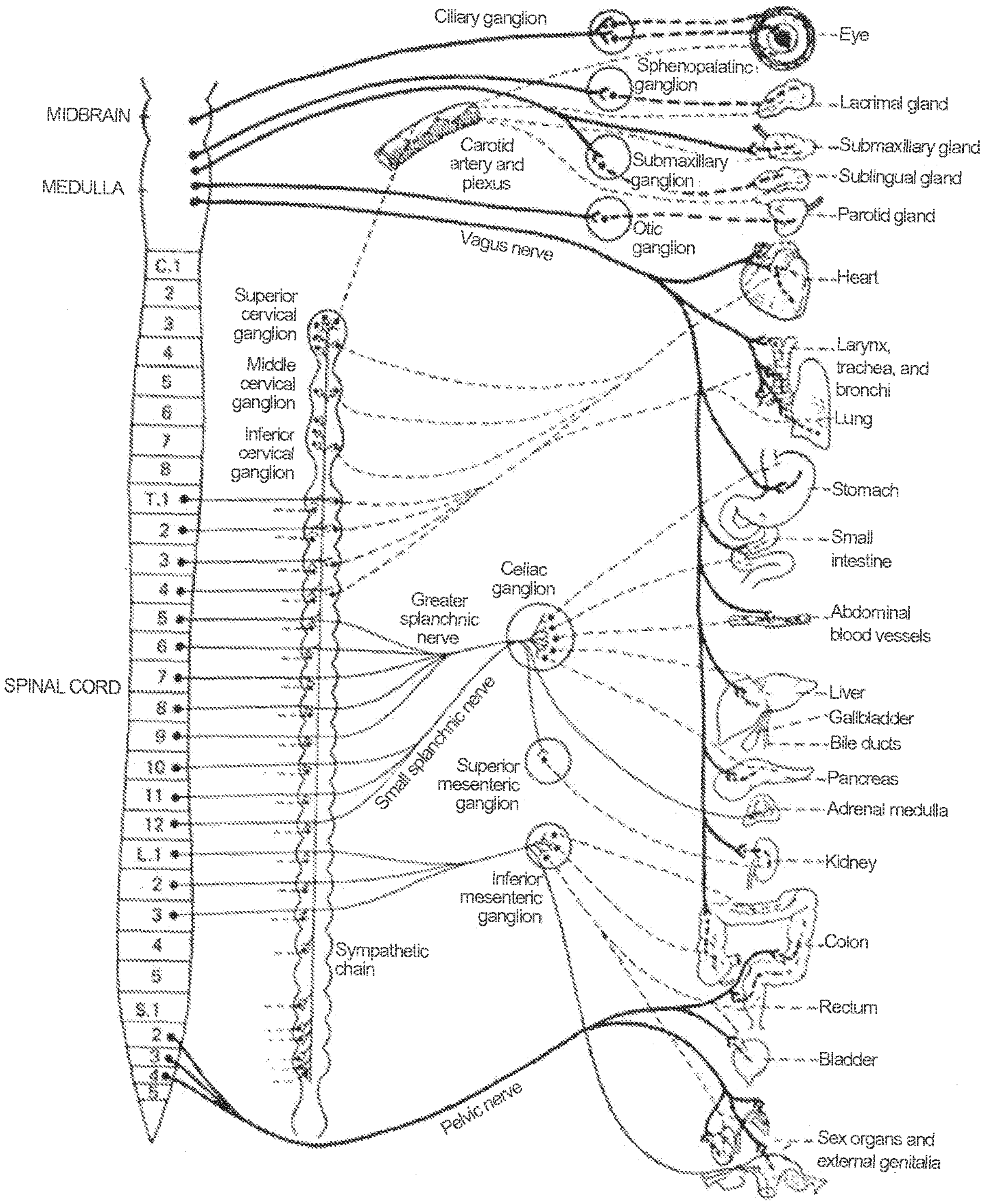
Ciliary ganglion
Eye
Sphenopalatine ganglion
Lacrimal gland
MIDBRAIN
Carotid artery and plexus
Submaxillary ganglion
Submaxillary gland
Sublingual gland
MEDULLA
Otic ganglion
Parotid gland
Vagus nerve
Heart
C.1
Superior cervical ganglion
Middle cervical ganglion
Larynx, trachea, and bronchi
Lung
Inferior cervical ganglion
Stomach
T.1
Small intestine
Celiac ganglion
Greater splanchnic nerve
Abdominal blood vessels
SPINAL CORD
Liver
Gallbladder
Bile ducts
Small splanchnic nerve
Superior mesenteric ganglion
Pancreas
Adrenal medulla
L.1
Kidney
Inferior mesenteric ganglion
Colon
Sympathetic chain
S.1
Rectum
Bladder
Pelvic nerve
Sex organs and external genitalia

FIG. 6

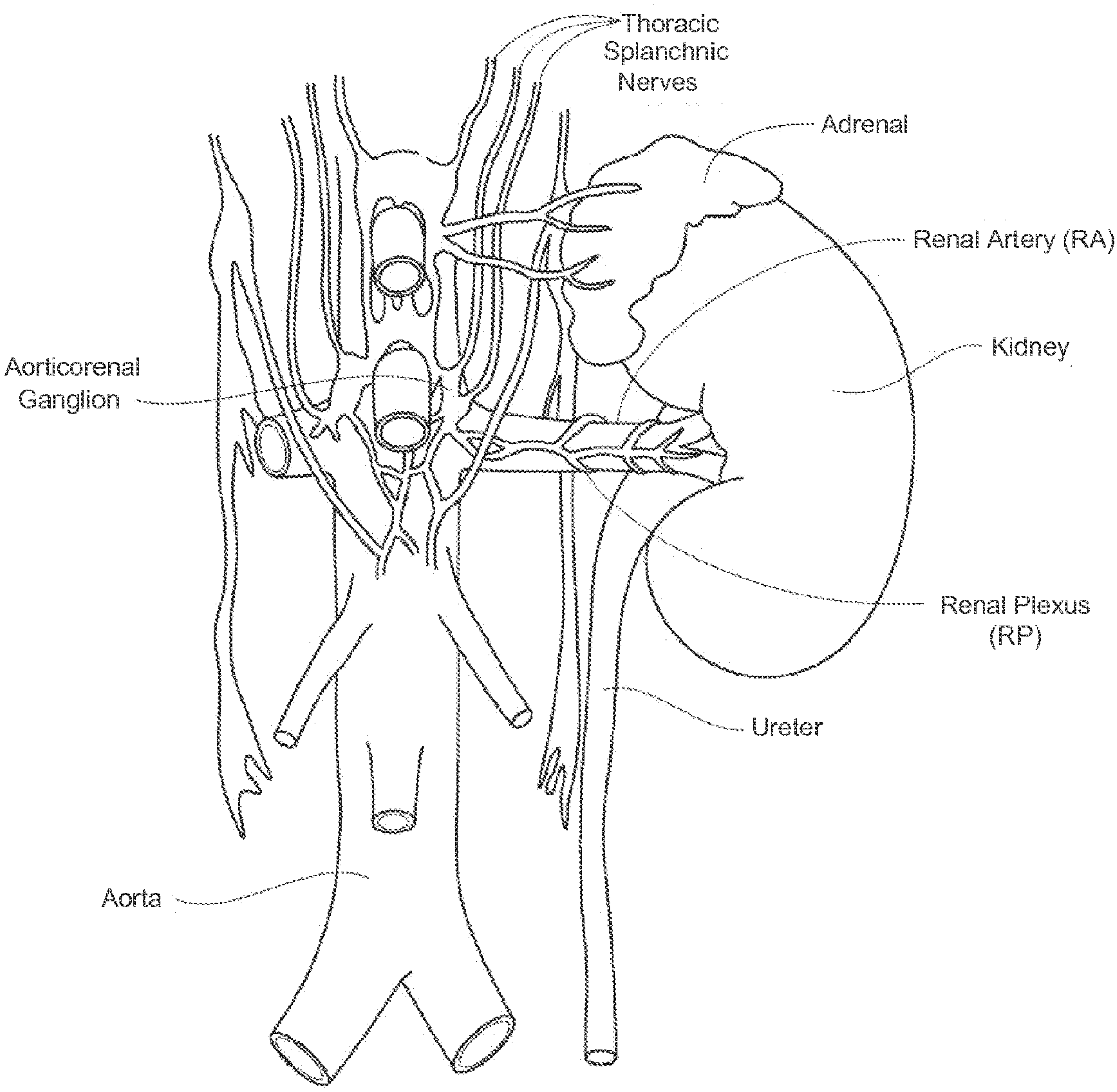
Thoracic
Splanchnic
Nerves
Adrenal
Renal Artery (RA)
Kidney
Aorticorenal
Ganglion
Renal Plexus
(RP)
Ureter
Aorta

FIG. 7

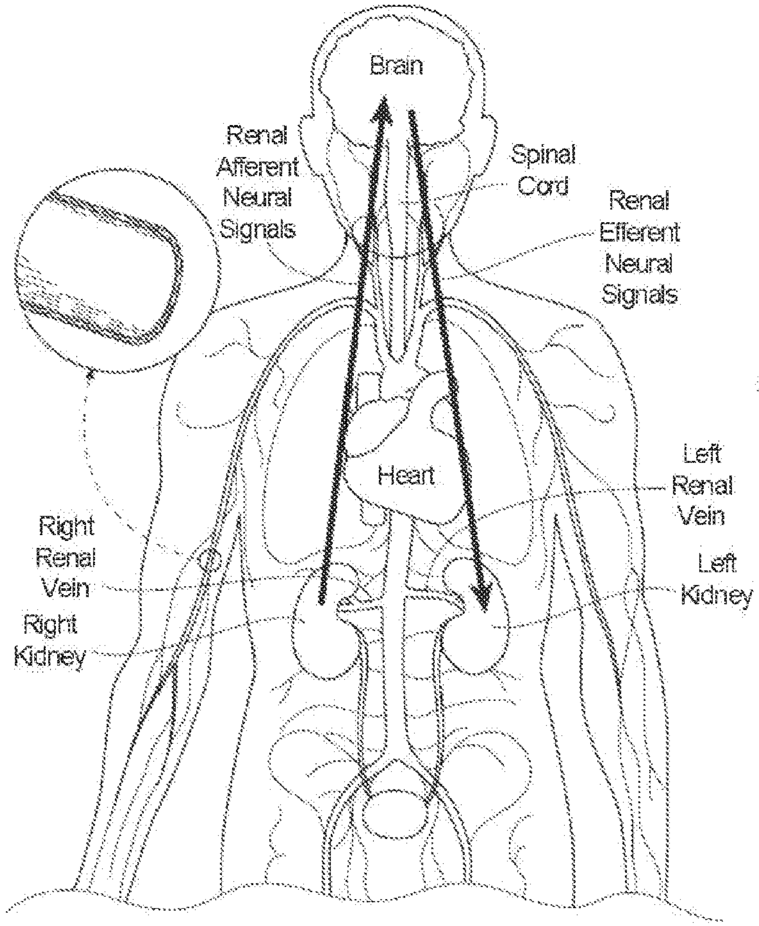
Brain
Renal Afferent Neural Signals
Spinal Cord
Renal Efferent Neural Signals
Heart
Left Renal Vein
Left Kidney
Right Renal Vein
Right Kidney

FIG. 8A

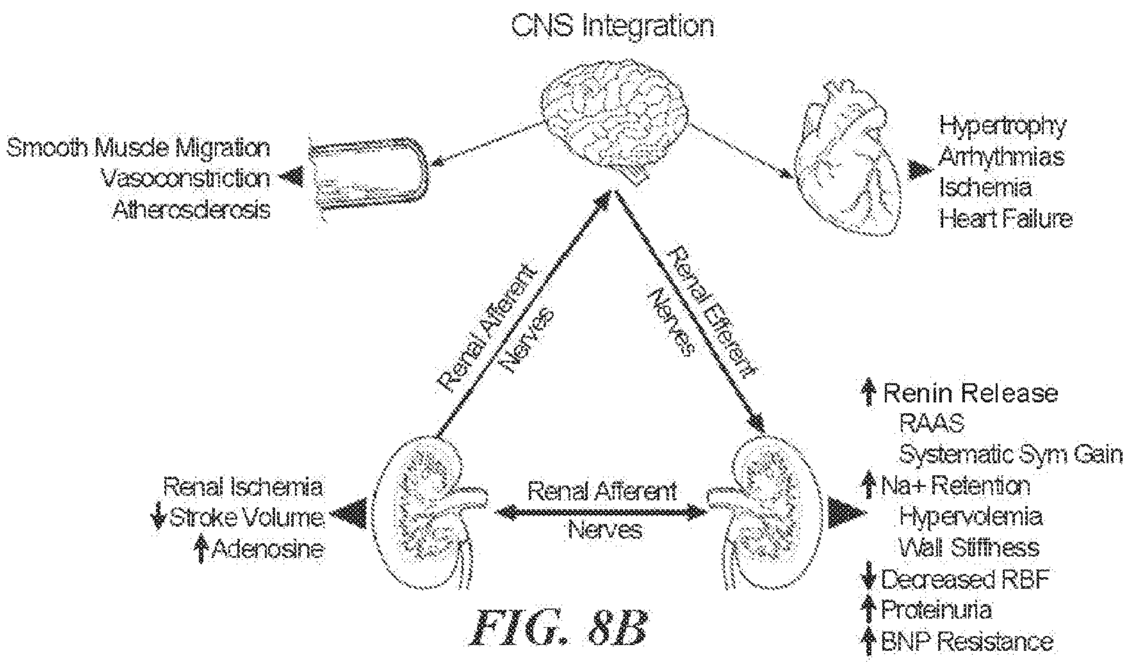
CNS Integration
Smooth Muscle Migration
Vasoconstriction
Atherosclerosis
Hypertrophy
Arrhythmias
Ischemia
Heart Failure
Renal Afferent Nerves
Renal Efferent Nerves
↑Renin Release
RAAS
Systematic Sym Gain
↑Na+ Retention
Hypervolemia
Wall Stiffness
↓Decreased RBF
↑Proteinuria
↑BNP Resistance
Renal Ischemia
↓Stroke Volume
↑Adenosine
Renal Afferent Nerves

FIG. 8B

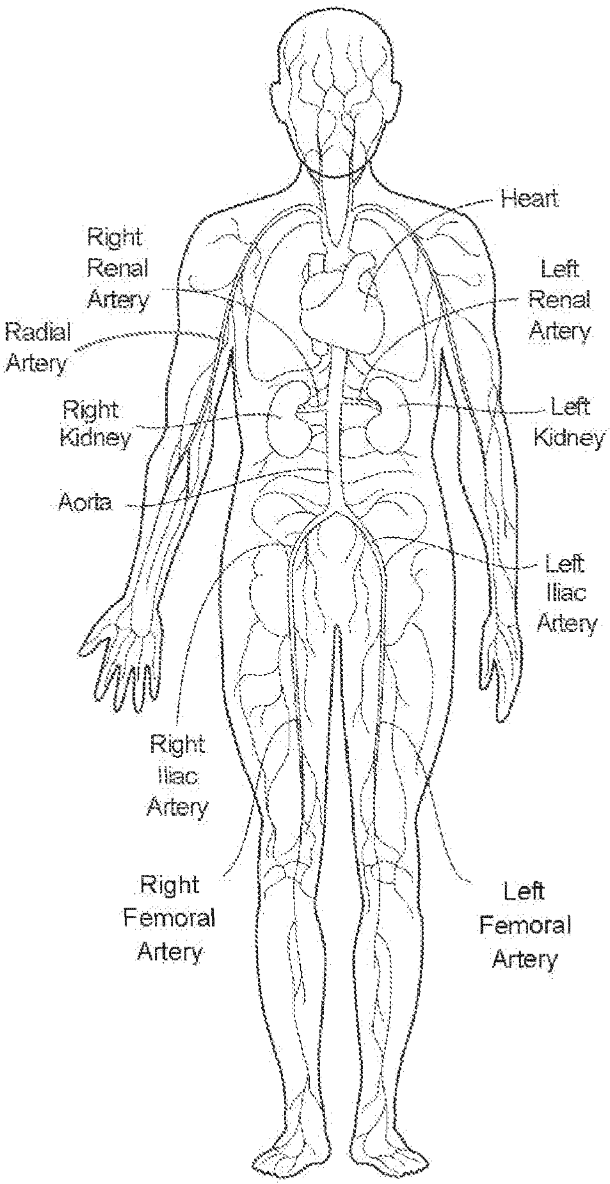

FIG. 9A

Arterial Vasculature

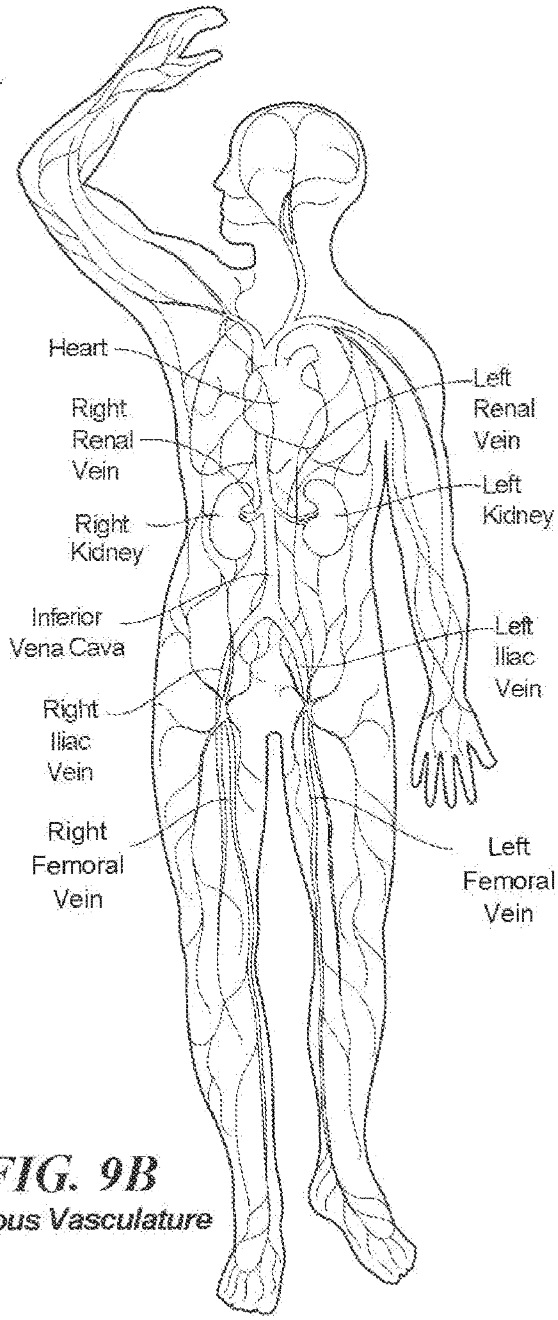

FIG. 9B

Venous Vasculature

Europäisches Patentamt
European Patent Office
Office européen des brevets

EUROPEAN SEARCH REPORT

Application Number
EP 16 19 7774

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	WO 2012/061161 A1 (MAUCH KEVIN [US]; CHANG WILLIAM [US]; GOSHGARIAN JUSTIN [US]; RIVERA L) 10 May 2012 (2012-05-10) * Title * * paragraph [0218] * * paragraph [0229] - paragraph [0232]; figures 15a-b,4b * * paragraph [0020] - paragraph [0202] * * paragraph [0138] * * paragraph [0309] * * paragraph [0113] * * paragraph [0098] * -----	1-13	INV. A61B18/14 A61M25/01 ADD. A61B18/00 A61M25/09
A	US 2001/023365 A1 (MEDHKOUR ADEL M [US] ET AL) 20 September 2001 (2001-09-20) * paragraph [0033] * -----	1-11	
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